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**INVESTIGATIONS**  
**ON**  
**EPIDEMIC INFANTILE PARALYSIS**

***REPORT***

FROM

**THE STATE MEDICAL INSTITUTE**

OF

**SWEDEN**

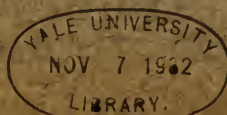
TO

**THE XV INTERNATIONAL CONGRESS ON HYGIENE AND DEMOGRAPHY,  
WASHINGTON 1912**

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**PUBLISHED BY THE STATE MEDICAL INSTITUTE**

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NORDISKA BOKHANDELN  
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TRANSLATED INTO ENGLISH  
BY  
ALFRED V. ROSEN, M. D.



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## Introduction.

Last year our country was visited by the largest epidemic of infantile paralysis that has ever appeared in Sweden. During the course of the year about 3800 cases were observed. Already early in the summer the cases were becoming remarkably numerous and in August they had reached an alarming number. Our knowledge of the disease had, it is true, lately been increased very considerably, thanks chiefly to experimental investigations, but the manner of transmission of the infection was still very little known, although after WICKMAN's thorough studies of the large Swedish epidemic of 1905, many things argued in favour of the probability of a transmission from one person to another. The need of definite, rational measures calculated to prevent, if possible, the spread of the disease made itself more and more felt. But as suitable instructions for such measures cannot be worked out without a knowledge of the origin and manner of propagation of the infection, the Royal Board of Directors of the Medical Department charged the Bacteriological Department of the State Medical Institute to investigate the manner in which the infection is transmitted. This investigation was started early in September last year.

As lately the observations speaking in favour of the disease being infectious have continued to increase it

is obviously necessary to presume that the patient himself is an important source of infection, even if not the only one. By means of experimental investigations in the last few years it has been proved also that the virus is to be found in several places in the interior of the body. On this account it seemed most important, in the first place, to investigate whether the virus was to be found in such parts of the body, e. g. on the mucous membranes, whence it might easily be spread. As it seemed possible to make a more thorough investigation of certain mucous membranes on the dead than on the living, we commenced our investigations on subjects recently dead from acute epidemic poliomyelitis. The results obtained induced us to continue the investigations on living persons: cases of typical infantile paralysis, abortive cases and healthy individuals. Our attention has been directed also to the possibility of a transmission through dead objects and living animals, blood-suckers as well as others. The considerable material of poliomyelitis in monkeys which these investigations have offered, has given us an occasion to more closely study the symptomatology and also the histological changes found in the spinal cord in connection with experimental poliomyelitis in monkeys. We have also studied the changes present in those mucous membranes of man, on which we have found the microbe of infantile paralysis as well as in the glands belonging thereto. Finally the epidemic of last year has been subjected to a close study from an epidemiological point of view.

The greater number of the persons who have been the subject of our investigations have been in-patients at the Epidemic Hospital of Stockholm. To the Medical Superintendent, Dr. Thure Hellström. who has

kindly placed his large material at our disposal and thereby greatly facilitated our work, we submit our sincerest thanks.

Also the following colleagues, Dr. J. Ehinger, Linköping, Dr. C. O. Elfström, Sundsvall, Dr. Hj. Forssner, Stockholm, Dr. Hj. Fries, Stockholm, Dr. I. Heineman, Stockholm, Dr. A. Fürstenberg, Stockholm, Dr. O. Lundborg, Jönköping, Prof. Dr. O. Medin, Stockholm, Dr. E. Sifversparre, Mariefred, Dr. O. Sjöberg, Eksjö, Dr. F. Svensson, Stockholm, Dr. K. G. Tingwall, Uppsala, Dr. Hj. Wennerberg, Gothenburg, and Dr. O. Westerberg, Rimbo, all of whom have transferred to us suitable cases or [in some other manner provided us with material for the experimental and pathological investigations, we beg to offer our sincere thanks.

Lastly, we are indebted to the great number of Swedish colleagues who have contributed material for an epidemiological investigation of the last epidemic in Sweden.

Dr. W. H. Trethowan from London has kindly assisted in the reading of the proof-sheets and made many valuable suggestions as regards the English terminology. We offer him our best thanks.

The drawings are by Miss A. Dahlgren, Stockholm.

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## A. Experimental and pathological investigations.

### I. The presence of the microbe of Infantile Paralysis in human beings.

By

*Carl Kling, Alfred Pettersson and Wilhelm Wernstedt.*

#### a) A review of the investigations previously made regarding the presence of the virus in the human body.

On Dec. 18, 1908, LANDSTEINER and POPPER communicated to the *K. K. Gesellschaft der Ärzte* in Vienna that they had succeeded in transferring poliomyelitis from human beings to monkeys. With this report the investigations on infantile paralysis entered a new era. Very soon reports of similar successful transmissions were made by KNOEPFELMACHER, FLEXNER and LEWIS, LEINER and v. WIESNER, RÖMER and others, and in the different laboratories an ardent study of the disease now commenced, monkeys being employed in the experiments. Thanks to these investigations our knowledge of infantile paralysis has deepened within the last three years in a previously unexpected manner and much in the hitherto quite obscure etiology has in this way become lucid.

The first fundamental experiments were made by LANDSTEINER and POPPER in November 1908. The material for their investiga-

tions was obtained from a 9 year's old boy who had died of poliomyelitis after 4 days' illness. Pieces of the spinal cord, removed shortly after death, were ground up in sterile, physiological saline solution and the emulsion injected into the peritoneal cavity of a *Cynocephalus hamadryas* and a *Macacus rhesus*. The Baboon was found lying very ill on the bottom of the cage on the 6:th day after the injection, and it died on the 8:th day. At the autopsy the internal organs were found to be perfectly normal, the spinal cord, on the other hand, on microscopic examination presented great changes. The pia mater showed more or less marked cellular infiltration, the grey matter being soft, oedematous and presenting the signs of an intense inflammation in the form of close or scattered perivascular and diffuse cellular infiltrations. The ganglion cells, especially those of the anterior horns, were badly damaged, almost destroyed, vacuolated and invaded by mononuclear and polymorphonuclear round cells. Also in the medulla oblongata, pons, cerebral peduncles and cerebral cortex were analogous inflammatory infiltrations found. The other experimentally inoculated monkey was observed 17 days after the injection to be paralyzed in both hind legs, which hung limp when the animal was lifted up. It was killed two days later and the changes found in the nervous system resembled precisely those in the other monkey, though they were less intense. With the spinal cord of this *Macacus* an attempt was made to inject three other monkeys but these remained well.

Thus was it proved, that, by means of an injection of the substance of the spinal cord taken during the acute stage of poliomyelitis, it is possible to produce in monkeys a disease which is both clinically and pathologically quite analogous to that occurring in human beings. Further the inflammatory changes found in the spinal cords of the infected animals spoke in favour of the disease having been caused by some infectious agent and not by a toxin, even though the real proof of this, viz. the inoculation from one animal to another, was still wanting. LANDSTEINER and POPPER tried to procure this evidence but did not succeed in doing so



on this occasion. In spite of very minute investigations, and employing the common bacteriological and cultural methods the authors could not demonstrate the presence of any bacteria in the spinal cord of the dead boy. They therefore considered it probable, that poliomyelitis is caused by some invisible virus, belonging to the protozoa.

The proof just referred to of the infectiousness of the disease was not long in appearing. In several places investigations on this point were started and towards the end of 1909 communications came almost simultaneously from FLEXNER and LEWIS, LANDSTEINER and LEVADITI, RÖMER, and LEINER and V. WIESNER, that they had succeeded in transferring the infection from one monkey to another by means of an emulsion of the spinal cord. The last mentioned authors had already then reached as far as the 6:th generation. Through this inoculation from one animal to another it was consequently established, that the lesions in the central nervous system are due to some living virus and not to a lifeless poison.

After this followed a number of works by the investigators above mentioned regarding the nature and qualities of the virus, but we need not dwell upon this matter here. One important observation, however, which was soon made by LANDSTEINER and LEVADITI as well as by FLEXNER and LEWIS and which has also been verified by other poliomyelitis experimentalists, must be emphasized viz. that the microbe of infantile paralysis is a *filtrable virus*, passing through filters such as the Berkefeld, Pukall, Reichel and Chamberland. The microbe seems to pass through more or less easily, but is partly retained even by a Berkefeld filter, judging from the fact that the infection with

filtered virus is less constantly successful, the period of incubation also being usually prolonged. In this connection the observation made by LANDSTEINER and LEVADITI as well as by FLEXNER and LEWIS, viz. that the virus may be *preserved in glycerine*, should here be mentioned, the infective agent in this respect thus resembling the virus of Vaccine and Rabies.

Of greater interest in regard to the question of how poliomyelitis is spread is the knowledge of the prevalence and distribution of the microbe in the organism.

Having demonstrated the presence of the microbe in the spinal cord and brain during the acute stage, investigations on the infectivity of the fluids and organs of the body were soon commenced in order to obtain some definite idea of the manner in which the virus gets into the body. The clinical and epidemiological experiences pointed to the mucous membranes of the upper respiratory and digestive passages as the seat of entrance, and the investigations were therefore in the first place directed to these localities. FLEXNER and LEWIS removed pieces of the mucous membranes of the nose of a monkey, which had just become paralyzed after an intracerebral infection, made an emulsion with physiological saline solution, filtered the same through a Berkefeld filter and inoculated it into a monkey in the usual way. The experimentally injected animal developed paralysis. By this experiment they proved that the virus of poliomyelitis had been deposited in the mucous membrane of a monkey, into which the virus had been introduced intracerebrally. From this experiment the conclusion was drawn, that the virus is eliminated through the mucous



membrane in question and that in all probability the same applies to human beings also.

To prove the correctness of this hypothesis it is necessary however that the presence of the virus be demonstrated also in secretions of the mucous membranes. But this gap in the chain of evidence seemed at first difficult to fill.

LANDSTEINER and LEVADITI tried to infect monkeys with the nasal secretions from two persons who had recently been suffering from poliomyelitis, and with nasal and pharyngeal mucus and saliva from recently paralyzed monkeys, without being able to induce the disease. LEINER and WIESNER made a similar attempt with the nasal secretion from a child who had died of poliomyelitis in the acute stage, but also this experiment gave a negative result. RÖMER had the same experience on inoculating monkeys with the saliva and buccal secretion of children attacked by poliomyelitis. STRAUSS wiped the mouth and pharynx of 10 patients suffering from infantile paralysis with swabs of cottonwool, washed these in physiological saline solution, filtered through a Berkefeld or Chamberland filter and injected 2—4 c. c. of the filtrate intracerebrally into monkeys, but all the animals remained well. During the epidemic of infantile paralysis in Massachusetts 1910—1911 ROSENAU, SHEPPARD and AMOSS made similar experiments. In 18 recent cases the mouth, nose and pharynx were washed with a saline solution, the fluid passed through a Berkefeld filter and injected both intracerebrally and intraperitoneally into monkeys. 15 of the animals showed no symptoms of disease; one died of generalised tuberculosis; in two of them, pareses developed after a few days, but these were found to be due, in the one case to a haemorrhage and in the other to a secondary infection at the seat of injection into the brain. Thus the presence of the virus in the secretions could not be demonstrated, but the authors, nevertheless, were still of the opinion that the virus might have been present in the secretions, though in such small quantity as not to give rise to paralysis. GINS inoculated without any effect a *Macacus* with the nasal secretion from a child dead from poliomyelitis.

*All attempts to demonstrate the presence of the microbe of infantile paralysis in the secretions from the mouth,*

*pharynx and nose of both human beings and monkeys had thus hitherto been unsuccessful and the question whether these secretions were a source of infection or not was still open.*

During some of the epidemics of infantile paralysis the observation has been made that gastro-intestinal disturbances not seldom occur at the beginning of the disease, before any pareses have yet appeared. Changes in the mucous membranes of the intestinal canal, such as hyperaemia and swelling of Peyer's patches and the solitary follicles have in fact been found rather often at the autopsy. Some investigators (KRAUSE and others) have therefore been inclined to consider the mucous membrane of the intestine as the seat of entrance of the infection. But the first experimental attempts to demonstrate the presence of the microbe in that membrane in order to support this view did not lead to the desired result.<sup>1</sup> LANDSTEINER and LEVADITI could not bring on poliomyelitis with a Berkefeld filtrate of the faeces of a monkey. The experiments by LEINER and v. WIESNER gave a similar result; neither could the microbe be found in the intestinal mucous membrane of the paralytic monkey. STRAUSS examined the intestinal contents of a human being attacked by poliomyelitis but found it non-virulent.

Interesting are the observations made regarding the prevalence of the virus in some of the lymphatic glands connected with the mucous membranes above mentioned. FLEXNER and LEWIS report, that they have succeeded in demonstrating the presence of the microbe in the mesenteric lymphatic glands of a child that died from

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<sup>1</sup> LEINER and v. WIESNER, however, by means of successful *experiments* on animals have shown that this way of infection is at least possible in monkeys.

poliomyelitis. According to the experience gained by RÖMER and JOSEPH these glands contain the virus also in monkeys. LEINER and v. WIESNER have examined the lymphatic glands of paralyzed monkeys and established the fact that the cervical, submaxillary and the mesenteric glands are virulent. LANDSTEINER, LEVADITI and PASTIA found that the microbe existed in the tonsils and pharyngeal mucous membranes of a child that died of poliomyelitis. The case on which they gained this experience was of interest from an epidemiological point of view since it commenced with distinct symptoms of an angina lacunaris, which, according to the view held by the authors, makes it probable that the virus had entered through the mucous membrane of the pharynx. The salivary glands of monkeys attacked by poliomyelitis have likewise been examined. The statements with regard to the existence of the virus in these organs differ, however, LANDSTEINER and LEVADITI succeeding in transferring poliomyelitis through this material, while on the other hand LEINER and v. WIESNER as well as RÖMER, did not. With regard to the liver and the bile all the investigators are of the same opinion, inasmuch as no one has succeeded in demonstrating the presence of the virus therein.

In explaining the spread of the contagion of infantile paralysis the possibility of a transmission by means of blood-sucking animals has been considered. Such a hypothesis, however, presupposes the existence of the microbe in the blood. What do the experiments on animals show with regard to this point? Such investigations have, it is true, not yet been made on any large scale, but those already performed show that the presence of the microbe can only with difficulty be demonstrated in the blood. Neither LANDSTEINER

NER and LEVADITI nor RÖMER succeeded in transferring poliomyelitis from monkey to monkey by means of blood. FLEXNER and LEWIS succeeded in getting a positive result but only by using as large quantity of defibrinated blood as 20 c. c., with 2 c. c. they failed. LEINER and V. WIESNER made 6 attempts with defibrinated monkey-blood taken either during the latent period or after the appearance of the paresis and one with the blood from a paralyzed child. Only in one case (from a monkey) did the infection succeed. Thus the virus seems not to be constantly present in the blood, and, when it is found there, only in small quantities. Nor has the presence of the microbe as yet been demonstrated in blood-forming organs such as the bone-marrow and the spleen.

*The microbe had thus been found to exist in the central nervous system, in the mucous membranes of the nose of monkeys, in the tonsils and pharyngeal mucous membranes of human beings, in some of the lymphatic glands of man and monkeys, in the salivary glands of monkeys and, exceptionally, in the blood.* But, on the other hand, it had as yet been searched for in vain in the buccal, pharyngeal and nasal secretions of both human beings and monkeys attacked by the disease, in the mucous membrane of the intestine and in the intestinal contents. Consequently when we commenced our investigations in the early part of September last year, we did not entertain any great hope of succeeding in solving some of the difficulties which had beset previous investigators but the result surpassed our expectations, and already on Sept. 19 before the Svenska Läkarsällskapet<sup>1</sup> we could demonstrate three paralytic

<sup>1</sup> The result of our investigations have partly been published in a bridged form in Zeitschr. f. Immunitätsforschung. Vol. 12.



monkeys which had been injected with a filtered secretion from the mouth, nose and pharynx, the trachea and the intestinal mucous membrane of persons who had succumbed to infantile paralysis. A few months later LANDSTEINER, LEVADITI and DANULESCO reported that they had succeeded in causing infection by means of nasal secretion from a paralytic monkey.

#### b) Investigations on clinically positive cases.

In order to effect a more thorough washing of the mucous membranes and partly also in order to obtain secretion from such mucous membranes from which it cannot at all be obtained during life, as f. instance the small intestine, or only with great difficulty, as f. instance that of the trachea, we commenced our investigations on dead bodies. The washing was done with saline solution as soon as possible after death. The oesophagus and the trachea having been ligatured, *the mouth, nose and pharynx* were first washed. Then an opening was made into the trachea below the ligature and repeated washings of the *upper air passages* were done by means of a pipette. Finally a small portion of the *small intestine*,  $\frac{1}{2}$ —1 m. in length, was removed just above the caecum. The intestinal contents having been pressed out of the intestine by passing it through the fingers, salt solution was poured into it, the ends closed and the mucous membrane thoroughly washed; this was repeated a few times. In most cases a piece of the spinal cord was also taken in order to serve as control inoculation.

Up to the time we began our investigations all attempts to demonstrate the virus of infantile paralysis in the secretions of the mucous membranes of

patients in various stages of the disease had failed. That the virus should be found on the mucous membranes could, however, be considered most probable. The negative result of the experiments might then be due either to too small a quantity of the secretion having been injected into the animals or else to the fact that through filtering, necessary in order to get rid of other kinds of bacteria that might give rise to disease the material used had become too poor in virus. We therefore considered it best to inject a rather large quantity of secretion, and for this purpose we have chosen the intraperitoneal method of injection, which makes it possible to introduce a comparatively large quantity of fluid. The injection into the peritoneum not giving, according to LEINER and v. WIESNER, nearly as good a result as the intraneural or intracerebral inoculation we have in most cases *combined the intraperitoneal injection with an inoculation into one sciatic nerve*. In some of the control injections only this latter method of inoculation has been employed.

At first the intraneural injection was always done under aether or chloroform anaesthesia. We soon, however, made the observation that the operation caused but very little pain, and in consequence we have lately entirely omitted the anaesthetic, chiefly in order to avoid, as far as possible, the onset of complicating pneumonias. Into the sciatic nerve 1 to 2 c. c. may easily be injected.

The investigations of LANDSTEINER and LEVADITI have proved that the microbe of infantile paralysis is partly retained even by a Berkefeld filter. The fluids we had obtained through washing were also observed to pass through rather slowly. It was there-

fore desirable to get a filter which allowed the fluid to pass more easily, while still satisfactorily retaining the common bacteria. All reasonable demands in this respect are fulfilled by HEIM's filter which when sufficiently tightly packed, transmits fairly freely even the specimens obtained from the mouth and nose, though sometimes rather mucous in character, at the same time filtering them sufficiently free from bacteria to prevent other bacterial infection.

In order to avoid an unnecessary sacrifice of animals each specimen has, as a rule, been injected only into one monkey. In those cases where the animal died suddenly without previously showing any symptoms, or where only non-characteristic signs have been observed, control inoculations with the spinal cord of the dead animals have been made on other monkeys.

Those animals which have been the subject of experimental inoculation have during life been observed daily and of those that died the internal organs and the seats of injection into the sciatic nerve and the peritoneum have been carefully examined at the autopsy, besides which microscopic examination of the spinal cord and in a few cases of the brain has been made. In a great number of cases the spinal cord of the dead monkeys has also been examined for bacteria by means of cultivation on the common nutritive media. Only from animals which died of acute pneumonia and pleurisy a few colonies of cocci were obtained. In the following accounts the result of the post-mortem examination, excepting that of the brain and spinal cord, is recorded only when distinct changes have been observed anywhere.

## 1) Investigations on dead bodies.

## Case I.

*Oscar Gunnar Efraim A—n*, a salior, 18 years of age.

Was taken ill on Aug. 29 in the evening; Aug. 31 in the evening, paralysis of the legs, temperature  $39^{\circ}$  C. Was on Sept. 1 admitted to Sundsvall's Epidemic Hospital; suffered then from paralysis of both legs, paresis of both arms, paresis of the bladder and commencing respiratory paralysis. Died the same day. Post-mortem examination Sept. 4.

Of the specimen obtained from *the buccal and nasal cavities* about 80 c. c. were passed through a Heim filter and injected intraperitoneally into *Macacus rhesus* no. 9, on Sept. 6. The animal was observed for several months, but no signs of paralysis could be detected.

About 50 c. c. of the specimen obtained from the *trachea* were passed through a Heim filter and, on Sept. 6, injected intraperitoneally into *Macacus rhesus* no. 7. Sept. 17, paralysis of left hind leg. Sept. 19, paralysis of both hind legs. Sept. 29, runs better, only left leg dragging behind. Sept. 30, lies on the bottom of the cage, scarcely moving. Died in the afternoon.

The pia mater of the brain vividly injected, the cortex markedly hyperaemic; on section the surface is very moist and congested. The vessels of the pia of the spinal cord greatly distended in the lumbar region; on section the spinal cord does not swell but is moist, the grey matter not hyperaemic, its boundary indistinct. Microscopic examination of the spinal cord: Hyperaemia, moderate, diffuse cellular infiltration of the grey matter, marked perivascular infiltration in the grey as well in the white matter; some ganglion cells rather well preserved, but a large number degenerated, showing a homogeneous, deeply stained, vacuolated cell body, often to a great extent attacked by leucocyte-neuronophagias; some ganglion cells almost completely destroyed. The changes most intense in the lumbar cord.

The fluid obtained from the *intestine* was first filtered through a Heim filter and then through a Berkefeld. Of the filtrate 50 c. c. were, on Sept. 7, intraperitoneally injected into *Macacus rhesus* no. 8. Sept. 16, paralysis of both fore legs, falls down when trying to walk. Sept. 18, lies on the bottom of the cage, moves very little,



cannot rise. Sept. 19, completely paralyzed, cannot move, but chews the food given it, panting respiration. Sept. 21, dead.

Well marked hyperaemia of the membranes of both brain and spinal cord, the section of the cord swells moderately, is moist; the grey matter rises above the surface and shows a distinct reddish discoloration. The changes most marked in the cervical portion of the cord. The microscopic examination shows hyperaemia and haemorrhages, oedema, distinct, diffuse and especially perivascular round-cell infiltration, most of the ganglion cells degenerated, some almost entirely disintegrated, of others there remain only dark, irregular elements; the changes most marked in the lumbar region.

The monkey which was inoculated with the specimen from the buccal cavity, showed no symptoms of paralysis, but those inoculated with the fluid from the trachea and the intestine showed, after the expiration of the ordinary period of incubation, characteristic of experimental poliomyelitis, distinct paralyses, the one dying on the 13:th, the other on the 6:th day after the onset of the disease. The histological changes found in the spinal cord were in both cases similar to those observed in acute poliomyelitis of monkeys. The period of incubation was in both cases about the same although the tracheal secretion was passed through a Heim filter, while the intestinal fluid was filtered both through a Heim and a Berkefeld. Thus the virus of infantile paralysis has been demonstrated in the secretions obtained from the trachea as well as from the intestine of the dead patient. Whether the buccal secretion contained any virus is uncertain. The fact that the monkey was not attacked, need not imply the absence of virus in the irrigation fluid.

## Case II.

*Gunnar S—t*, a schoolboy from Upsala, aged 14.

He caught the infection in Dalarne, where during the summer cases of infantile paralysis had occurred in the farm next to his own home. After arrival in Upsala he fell ill with slight fever and general symptoms on Aug. 30—31; had possibly been unwell for some days previously. On Aug. 31, in the evening, slight paraesthesiae of arms and fingers were observed as well as some slight degree of incoordination in the movements of the fingers and hands. Sept. 1, no isolated, fully distinct paresis as yet to be observed. During Sept. 1—2 the pareses and signs of incoordination increased somewhat. During the night of the 3:rd of Sept., the patient awoke with a feeling of distinct difficulty of breathing accompanied also by a considerable weakness of the arms. After that the symptoms quickly increased, until he was admitted to the Epidemic Hospital of Upsala in the morning. Was then suffering from severe inspiratory dyspnoea (no cyanosis), the diaphragm evidently paralyzed, the left arm highly paretic, the right one less, the facial and hypoglossal nerves not affected. Could swallow tolerably well, slight laryngeal paralysis. The legs not markedly affected. Mind clear, no depression nor somnolence. Quick progression of the symptoms; died in the forenoon. Post-mortem examination on Sept. 4.

The fluids from the *mouth and nose* were filtered through a new Berkefeld filter, and 40 c. c. of the filtrate injected intraperitoneally into *Macacus rhesus* no. 4, on Sept. 5. Sept. 19, paralysis of the right hind leg. Sept. 24, the power of motion of the leg improved, but the animal cannot grasp with the left hand, is, however, able to move the arm. Oct. 8, holds the left hand closed, when running drags the right hind leg, climbs badly. The condition remained unchanged until Dec. 10, when the monkey was lying on the bottom of the cage, moving but very little and unable to rise. Dec. 11, dead. Through a mistake the monkey was destroyed before the autopsy was made.

15 c. c. of the *tracheal* fluid were passed through a Heim filter and injected into the peritoneal cavity of *Macacus rhesus* no. 6, on Sept. 6. The animal was observed for several months but showed no symptoms of disease.

The *intestinal* fluid was filtered through a Berkefeld filter and

40 c. c. were injected intraperitoneally into *Macacus rhesus* no. 3, on Sept. 5. The animal was found dead on Nov. 10.

The membranes of the brain and the spinal cord vividly injected. On section the spinal cord swollen, the grey matter deeply reddish-grey. Microscopic examination of the cord showed considerable hyperaemia, oedema and haemorrhages, the latter in some places rather large; no cellular infiltration; commencing hypertrophy of the glia cells; the greater part of the ganglion cells deeply stained, shrunken, with the protoplasm homogeneous and vacuolated; karyolysis.

On Nov. 15, *Cercopithecus Burnetti* no. 148 was injected into the peritoneum and left sciatic nerve with an emulsion of the spinal cord belonging to monkey no. 3, filtered through a Heim filter. Nov. 22, the animal climbs slowly and jerkily, holding the hind legs crooked when running. Died on Nov. 25.

The pia of the brain vividly injected, but the surface of the spinal cord pale; the section only slightly swelling, the grey matter sharply marked, greyish-red. The microscopic examination showed no other changes, than that some of the ganglion cells were somewhat deeply stained and homogeneous.

About 2 grammes of the *spinal cord* obtained from the deceased boy was made into an emulsion that was passed through a Heim filter, and, on Sept. 6, injected into the peritoneum of *Macacus rhesus* no. 5. Sept. 15, paresis of the right arm. Oct. 8, complete paralysis of the right arm, which hangs flaccid along the side of the animal when running or climbing. The condition did not change during the nearest time following.

Although the monkey which had been infected with the fluid obtained from the mouth, was not, owing to an oversight, submitted to autopsy, and consequently the cord not examined, it may, however, on account of the clinical picture presented, with the greatest probability be assumed, that the animal had suffered from poliomyelitis which commenced a fortnight after the injection. In the same way, it seems very likely that the monkey No. 6 which was inoculated with the intestinal fluid, died from experimental poliomyelitis, although the changes were but small, and the nature

of the disease not ascertained through the control inoculation. The tracheal secretion, on the other hand, did not cause any symptoms in the experimentally injected animal. The monkey infected with the emulsion from the spinal cord developed a persistent, complete paralysis of one arm, but otherwise recovered completely, which possibly might be considered to be due to a low degree of virulence possessed by the microbe present in the person in question.

### Case III.

*Gustaf Alfred Henning V—n*, a boy of 6 years, Sundsvall.

Was attacked with febrile symptoms on Sept. 1. Sept. 2, temperature 39° C., pharyngeal paralysis. Admitted to the Epidemic Hospital on Sept. 4. On admission he was still only suffering from pharyngeal paralysis and fever, later on attacks of dyspnoea, general restlessness, vomiting and gnashing of teeth set in; died of respiratory paralysis on Sept. 4. Post-mortem examination the following day.

The fluid obtained by washing *the mouth*, amounting to about 55 c. c., was passed through a Heim filter and injected intraperitoneally into *Macacus cynomolgus* no. 23, on Sept. 18. Nov. 11, the animal runs and climbs somewhat slowly, is easy to catch. The same condition though somewhat aggravated prevailed until the last day of December. On Jan. 1 the monkey was found dead.

The surface of the brain pale, the vessels of the pia of the spinal cord somewhat injected, on section the surface of the cord swelled, no very sharp contrast between the white and the grey matter, the latter not reddish. Microscopic examination: Moderate hyperaemia and haemorrhages but no cellular infiltration, neither diffuse nor perivascular; the neuroglia cells generally large, clear, transparent without distinct processes, the majority of the ganglion cells of the medulla oblongata as well as of the spinal cord highly degenerated, some light blue, finely granular, transparent, apparently in a state of dissolution, others shrunken, irregular, deeply stained; often the large, clear cells of the surrounding glia



tissue have, so to speak, eaten their way into the degenerated ganglion cells.

The *tracheal* fluid, 30 c. c., was filtered through a Heim and, on Sept. 18, injected intraperitoneally into *Macacus cynomolgus* no. 22. Sept. 27, the animal looks ill and when let out on the floor, it walks with a limp, falling every now and then on its nose, commonly to the right; seems to be weak especially in the right hand. Died on Sept. 29.

The blood vessels on the surface of the brain moderately distended, the cortex in some places reddish. The vessels on the surface of the spinal cord are distinctly visible over the posterior aspect of the lumbar enlargement; on section the surface swells somewhat in the cervical and lumbar regions, the grey matter having a reddish tint, in the cervical cord the anterior commissure distinctly red. Microscopic examination: Moderate hyperaemia but no haemorrhages and no cellular infiltration; the glia cells large, clear and transparent; the ganglion cells to a very large extent degenerated, the nucleus diffusely and deeply stained, the cell body shrunken, deeply stained, homogeneous, vacuolated and as a rule much attacked by the large, clear cells in the neighbourhood; some nerve cells are pale, finely granular (Fig. 3).

With non-filtered emulsion of the spinal cord from the monkey no. 22 injections were, on Oct. 2, made into the left sciatic nerve of *Macacus cynomolgus* no. 55 and *Macacus rhesus* no. 56.

No. 55. Oct. 9. Complete paralysis of the right hind leg which is dragged along. Oct. 10, dead.

The vessels of the membranes of the brain rather markedly injected, the vessels on the surface of the cord slightly visible, the section swollen, moist, the grey matter showing a greyish-red discoloration with very distinct red spots and streaks, chiefly in the cervical region. Microscopic examination: Hyperaemia and haemorrhages, cellular infiltration in both pia and cord, in the latter place both diffuse, in groups and perivascular, some of the glia cells enlarged, clear, transparent. Some of the ganglion cells are pretty well preserved with a distinct tigroid substance, but the majority are more or less degenerated and often encroached upon by a large number of neuronophages, partly provided with a round nucleus, partly of polymorphonuclear type with a cell body but little differing from that of the nerve cell; in other places the

ganglion cells show exactly the same changes as those found in the preceding monkey no. 22 (Fig. 4).

No. 56. Oct. 12, complete paralysis of both hind legs, which are dragged along. Oct. 14, lying on the bottom of the cage, moving only head and arms a little. Oct. 16, dead.

The vessels on the surface of the brain and the spinal cord rather injected, a distinct contrast between the cortex and medulla, the grey matter of the cord of a deep greyish-red colour with plenty of spots and streaks. In the left lung a recent pneumonia and some caseating foci, varying in size from a hemp-seed to a pea. Microscopic examination of the spinal cord: Marked hyperaemia, oedema and solitary haemorrhages, moderate cellular infiltration arranged in groups in the grey matter, distinct perivascular infiltration; hypertrophy of some of the glia cells; the greater number of the ganglion cells of the spinal cord showing either granular degeneration, sometimes almost complete dissolution, or else being shrunken, deeply stained, homogeneous and attacked by the large, clear, surrounding glia cells; in the medulla oblongata where only a small number of the nerve cells show marked degeneration, the latter change is the more common one; no typical leucocyte-neuronophagias.

The *intestinal* specimen, 40 c. c., was, after having been filtered through a Heim, injected, on Sept. 16, into the peritoneum of *Macacus cynomolgus* no. 18. Oct. 14, climbs badly, does not stand well on the hind legs, is easy to catch. The general condition remained unaltered, or got perhaps a little worse, until Dec. 4, when the monkey was found on the floor of the cage, only able to move very slightly. Died Dec. 5.

The vessels of the pia mater of the brain and those of the surface of the cord vividly injected, a sharp contrast noticeable between the cerebral cortex and medulla, the section of the cord swelling, the grey matter of a pale greyish-red tint. Microscopic examination: Hyperaemia, haemorrhages, but no cellular infiltration; some of the glia cells enlarged, clear, transparent; a great number of the nerve cells shrunken, vacuolated, homogeneous, deeply stained and partly deeply infiltrated by the enlarged, clear, surrounding glia cells.

The monkey which had been inoculated with the fluid obtained from the trachea, was attacked on the 9:th day with paresis of the arms and died two days later. The spinal cord showed no cellular infiltration

and no neuronophagia due to leucocytes, but a progressive disturbance of the nutrition of the cells of the supporting tissue and an intense degeneration of the ganglion cells, the bodies of which were to a great extent attacked by the large, clear cells in the neighbourhood. The control monkey which had been inoculated with spinal cord from no. 22 showed both during life clinically typical paralysis, and after death perivascular cellular infiltration as well as leucocyte-neuronophagias in the cord. The fluid from the trachea must therefore have contained the virus of infantile paralysis.

With regard to monkey no. 23 which had been injected with the specimen obtained from the mouth and pharynx, some doubt may exist whether the animal was suffering from poliomyelitis, as it was not attacked until after the lapse of a period of incubation of seven weeks, and, besides this, the illness had a protracted course, extending for about the same length of time and characterized by muscular weakness without any distinct isolated pareses. The spinal cord, however, showed about the same changes as those found in the above mentioned monkey no. 22, and which through control inoculation were proved to be due to the microbe of infantile paralysis. And, besides, there is hardly any reason to doubt that the microbe should be found in the pharynx and the mouth when its presence in the trachea had been demonstrated, as the secretion from the latter physiologically gets into these cavities. The specimen from the intestine has also caused a comparatively chronic illness with histological changes in the cord similar to those observed in the two preceding cases. According to our opinion, the experimental investigation has thus with regard to

this case proved the presence of the virus of infantile paralysis on all the three mucous membranes examined.

#### Case IV.

*Carl Runo C—n*, aged 2, Stockholm.

Returned from Gärdsjö in Västergötland on Aug. 29. Onset of illness on Sept. 2 with fever and one attack of vomiting. In the same house another child had previously been attacked by infantile paralysis. Admitted to the Epidemic Hospital of Stockholm on Sept. 5. The general condition rather bad, apathetic, very pale. Some rigidity of the neck. The head falls to that side to which the patient is held; the arms can be moved but they appear to be weaker than normally, the legs are very flaccid, but he is able to extend them at the knee joints and perform plantar flexion of the feet; the patellar reflexes weak on the right, absent on the left side, the plantar reflexes lively. Sept. 7, more and more apathetic and unclear in his mind; the respiration labouring, chiefly of a costal type, the urine passed into bed. Sept. 8, grew unconscious at midnight, died in the morning. The urine taken at the autopsy the same day contained 4.5 % sugar, Gerhardt negative.

The fluid *from mouth and nose*, 40 c. c., was, after filtration through a Heim filter, on Sept. 12, injected intraperitoneally into *Macacus cynomolgus* no. 10. Oct. 15, the monkey lies on its side, paralyzed in both arms and legs, cannot rise. Oct. 16, dead.

The vessels on the surface of the brain are vividly injected, a marked contrast between cortex and medulla noticeable. The vessels of the spinal cord only slightly injected, the section swells considerably, the grey matter somewhat greyish-red, especially in the cervical enlargement. On microscopic examination the spinal cord shows hyperaemia and haemorrhages, but no cellular infiltration; hypertrophy of a great number of the glia cells; the majority of the ganglion cells are more or less degenerated, the nucleus as well as the cell body homogeneous and deeply stained, the latter often presenting deep indentations caused by the large, clear cells in the neighbourhood.

The *tracheal* fluid, 50 c. c., after having been passed through a Heim filter, was injected, on Sept. 12, into the peritoneum of *Macacus cynomolgus* no. 11. Sept. 30, runs somewhat joggingly and sway-



ing the body. The condition remained about unaltered till Oct. 11, when the animal was found limping a little in the left hind leg, Oct. 15, limps plainly in the left hind leg. Oct. 16, found dead.

The brain without macroscopic change. Hyperaemia of the vessels of the lumbar and dorsal portions of the cord, the spinal cord on section is moist and swollen, a distinct reddish discoloration of the grey matter noticeable, especially in the cervical, but also in the lumbar region. Microscopic examination: Distinct hyperaemia, haemorrhages in the cervical cord, and in some places oedema but no cellular infiltration, a smaller number of the glia cells enlarged, clear; the ganglion cells partly well preserved, partly highly degenerated, shrunken, homogeneous, deeply stained, extensively vacuolated and often attacked by the surrounding glia cells. The changes are most distinct in the cervical region and in the medulla oblongata.

The specimen obtained from the *ileum*, 25 c. c., was filtered through a Heim and, on Sept. 13, injected intraperitoneally into *Macacus cynomolgus* no. 13. Oct. 16, runs and climbs badly, when jumping the fore legs give way so that the animal falls on its nose. Oct. 17, climbs very slowly and badly, gait rocking, the legs now and then giving way, causing the animal to fall, sways the body back and forth when sitting, has difficulty in keeping hold with the hands. Oct. 19, perhaps a little livelier and somewhat stronger in the legs, on climbing, however, it sometimes loses its hold and falls rather helplessly on to the floor. Oct. 20, does not want to walk, when trying it falls to the left, can easily be pushed over, signs of paresis of the left hand. Oct. 21, found dying on the floor of the cage. Killed.

The brain presents no macroscopical change. No distinct injection on the surface of the spinal cord, the cord on section moist, not swelling, the grey matter somewhat reddish. Microscopic examination: Slight hyperaemia, solitary haemorrhages, especially in the commissure, no definite signs of cellular infiltration nor of hypertrophy of the glia cells; some of the ganglion cells have quite a normal appearance, others are shrunken, deeply stained and vacuolated, others again very pale and finely granular, as if in a state of dissolution.

An emulsion of the *spinal cord* of the dead body having been made and filtered through a Heim, 30 c. c. were injected intra-

peritoneally into *Macacus cynomolgus* no. 12, on Sept. 14. Sept. 27, the animal is found dead in its cage.

The pia of the brain and spinal cord hyperaemic, especially over the pons and medulla oblongata. The section through the cervical and lumbar enlargements swollen and moist, the grey matter showing a moderate degree of reddish discoloration with a few red spots and streaks, similar appearances also found in the medulla oblongata; the brain substance hyperaemic. Microscopic examination of the spinal cord: Hyperaemia but no haemorrhages, considerable cellular infiltration, both perivascular, diffuse and in groups in the grey matter; some of the cells of the glia large, clear and transparent; the greater part of the ganglion cells degenerated, others filled with neuronophages like those described in the case of the monkey no. 35.

All the three monkeys that had been injected with the fluids obtained by washing were, after a period of incubation of respectively 33, 18 and 4 days, attacked and developed distinct pareses. One died at the end of a relatively short period of illness, the other two after somewhat longer periods. In all three, degeneration of the ganglion cells was found, but no cellular infiltration and no leucocyte-neuronophagia. The latter changes were, on the contrary, found in the spinal cord of monkey no. 12, which had been inoculated with the spinal cord emulsion and which died suddenly after 13 days without presenting any signs of paralysis.

#### Case V.

*Siri Linnea E—n*, a girl of 11, from Stockholm.

Had since mid-summer, been staying in Vingåker where no case of infantile paralysis occurred during the summer, but some in September. Came home August 19. Onset Sept. 4, when at school, with chills, headache and fever up to 40° C., constipation, no vomiting, nor any cough or sore throat. No pareses observed, but her mind grew gradually less clear. Was admitted to the Epidemic Hospital of Stockholm, on Sept. 6. The general condition bad, the patient lying apathetic with an absent-minded, somewhat staring,

lustrous lock in her eyes, her neck stiff; signifies pain when her head is bent forward, replies hesitatingly and with a low, almost aphonic voice when spoken to, performs, on request, movements with the eyes and the tongue, but mostly after some hesitation or only at the second request. Power to move the arms and legs present, but she does not, owing to her state of mind, perform any movements when asked to; respiration quickened, costal in type. Patellar reflexes present, increased on the left side; the plantar reflexes abnormally lively, causing violent and quick movements of the legs which, besides, seem to be ataxic; abdominal reflexes present. The pharynx highly reddened.

On Sept. 7, temperature  $39.2^{\circ}$  C. in the morning, sensorium not clear, reacts for a moment when spoken to, seems to be disorientated, movements of eyes coordinated, marked opisthotonos, is able to move the lower extremities, respiration chiefly costal, the abdomen boatlike, retracted, swallows with difficulty, no apparent facial paresis, urine and faeces passed spontaneously, reacts to pin-pricks in the lower extremities, not in the upper ones; the patellar reflexes increased on the left side, almost absent on the right; Babinsky and Kernig negative. Rather profuse perspiration in the face. Since yesterday evening a change for the worse with regard to her general condition.

Sept. 8,  $38.9^{\circ}$  C. in the morning,  $40.6^{\circ}$  C. in the evening; unconsciousness gradually increasing. Died in the morning of Sept. 9. Post-mortem examination the same day.

The *intestinal* fluid was filtered through a Heim, and 40 c. c. of the filtrate injected intraperitoneally into *Macacus cynomolgus* no. 21, on Sept. 18. Oct. 6, does not climb willingly nor run quite naturally. Oct. 14, paresis of the left arm, walks very slowly, falling over to the left. Oct. 15, dead.

The surface of the brain moderately hyperaemic, the cortex in some places of a reddish colour. Hyperaemia in the lumbar region, on section the spinal cord swollen, everywhere moist, the grey matter reddish and dotted with red. Microscopic examination: Hyperaemia and haemorrhages in the spinal cord, but no cellular infiltration; the glia cells hypertrophied; the nerve cells to a great extent degenerated, shrunken, deeply stained, vacuolated, homogeneous and sometimes as though notched at the edges by the surrounding glia cells.

The animal injected was attacked after an incubation period of 18 days, developed a distinct paresis of one arm and died on the 11:th day after the onset of the disease. The spinal cord showed hypertrophy of the glia cells and degeneration of the ganglion cells, but no cellular infiltration and no leucocytic neurophagia.

#### Case VI.

*Einar L—l*, a boy of 4, from Stockholm.

Onset of disease on Sept. 2 with headache in the occipital region; he felt poorly and wanted to lie down, said he suffered from aching pains in the stomach. Was on Sept. 5 admitted to the Epidemic Hospital of Stockholm. The general condition pretty good, temper quickly changing, considerable stiffness of the neck, no pareses, the gait calls for no remark. The plantar and cremaster reflexes normal, the patellar, triceps and Achilles-tendon reflexes increased, abdominal reflexes absent on the left side. Nothing abnormal in the pharynx. Later on in the day hands somewhat shaky, when he is to perform any movements, the gait stiff and somewhat unsteady. Sept. 8, worse, pale and very restless, difficulty of breathing, complains of pains in the chest and abdomen. Dulness over the upper part of the right lung and large râles posteriorly, the left lung showing somewhat similar physical signs. Sept. 11, consciousness fully retained till yesterday, the difficulty of breathing increased, numerous hard râles were heard over the right lung; died this morning. Post-mortem examination the same day.

The fluid obtained from the *mouth, pharynx and nose* was filtered through a Heim, and 40 c. c. injected intraperitoneally into *Macacus cynomolgus* no. 15, on Sept. 13. Sept. 24, found dead in the cage; on Sept. 23, the animal had appeared bright.

The vessels on the surface of the brain, especially around pons and medulla oblongata distinctly injected; the same condition found at the posterior surface of the lumbar enlargement. The section through the medulla oblongata distinctly more congested than normally; on section the spinal cord is moist, especially in the cervical region, the grey matter showing a red discoloration as well as red spots. On microscopic examination the spinal cord shows hyper-



aemia and haemorrhages, here and there a slight cellular infiltration around the vessels, the latter everywhere containing plenty of white blood corpuscles; hypertrophy of the glia cells; a great number of the ganglion cells degenerated, shrunken, vacuolated, and homogeneous, the nucleus and cell body deeply stained, the latter in many places being attacked by the large, clear, surrounding cells.

The fluid obtained from the *trachea*, 40 c. c., was filtered through a Heim, and, on Sept. 13, injected into the peritoneum of *Macacus cynomolgus* no. 14. Sept. 20, runs badly, limps and is easy to catch. Sept. 24, still unwell, weak and powerless, is easy to catch, is able to climb, though very slowly. Oct. 27, found dead.

The vessels on the surface of the brain moderately distended. Along the whole of the spinal cord, the vessels are abnormally full, especially at the lumbar enlargement. Also the dura and the extradural tissues are hyperaemic. On section the spinal cord swells considerably, especially in the cervical region, the grey matter has a marked reddish tint, with distinct red spots and streaks. The medulla oblongata on section markedly congested, and the olivary body distinctly marked through a reddish discoloration. The microscopic examination shows considerable hyperaemia, oedema and diffuse haemorrhages throughout the spinal cord, in some places signs of perivascular cellular infiltration; hypertrophy of the glia cells; most of the ganglion cells highly degenerated and of same appearance as those found in the spinal cord of the preceding monkey, the surrounding large, clear glia cells often having eaten themselves deeply into them.

40 c. c. of the *intestinal* fluid were, after filtration through a Heim, injected intraperitoneally into *Macacus cynomolgus* no. 17, on Sept. 15. Found dead on Sept. 18. At the autopsy a small number of bacteria were found in the abdominal cavity, otherwise nothing abnormal.

Of the *spinal cord* of the dead boy an emulsion was made and 40 c. c. filtered through a Heim and injected into the peritoneum of *Macacus cynomolgus* no. 16, on Sept. 15. Sept. 30, runs rather unsteadily, joggingly and slowly, possibly weak in the left fore leg; is easy to catch. Oct. 4, shows about the same symptoms. Oct. 6, runs, walks and climbs very badly, with short steps, is easily pushed over. Oct. 11, dead.

The cortex of the brain of a reddish tint, the brain substance being in most places more than normally congested. The vessels



on the surface of the spinal cord moderately distended, the section of the cord considerably swollen in the cervical and lumbar regions, the grey matter being reddish, streaked with red and rising above the white matter. Microscopic examination of the spinal cord: Moderate hyperaemia and solitary haemorrhages as well as some oedema in the lumbar cord, but no cellular infiltration; hypertrophy of the glia cells; in the entire spinal cord most of the ganglion cells are highly degenerated, the nucleus diffusely and generally slightly stained, the cell body homogeneous, of a dark colour, vacuolated and shrunken and often greatly encroached upon by the surrounding large, clear cells.

In the spinal cords of the monkeys that had been inoculated with the specimens from the mouth and trachea, and had died, the one within two, and the other after about six weeks, a considerable degree of degeneration of the ganglion cells and slight signs of perivascular infiltration were observed, one of the animals also showing signs of general muscular weakness, from which it may correctly be assumed that experimental poliomyelitis was present. Neither did the monkey which was inoculated with the emulsion of the spinal cord develop any distinct, isolated paralysis but only general muscular weakness, the changes observed in the spinal cord being similar to those found in the above mentioned animals. The monkey that had been inoculated with the intestinal fluid died of peritonitis.

#### Case VII.

*Jenny Florida F—n*, a girl aged 8, from Stockholm.

Admitted to the Epidemic Hospital of Stockholm on Sept. 5. General condition bad, sensorium free; retraction of the head and of the back. Forward bending of the head causes pain; the pupils react to light, co-ordinated movements of the eyes, the look somewhat staring; the arms rather weak, especially the right one, legs perfectly flaccid, no abdominal or patellar reflexes, triceps

reflexes uncertain. Sept. 10, still conscious but looks worse, is exceedingly sensitive in the back and head; to-day also the left arm is very flaccid; died in the afternoon. Post-mortem examination on Sept. 11.

Of the fluid from the *mouth* and *pharynx* 50 c. c. were filtered through a Heim and, on Sept. 27, intraperitoneally injected into *Macacus cynomolgus* no. 38. Sept. 28, death. At the autopsy nothing was found excepting a small quantity of fluid in the abdominal cavity which contained a few leucocytes but no bacteria.

Of the *tracheal* fluid 40 c. c. were filtered through a Heim filter and, on Sept. 18, intraperitoneally injected into *Macacus cynomolgus* no. 24. Oct. 6, runs slowly, climbs badly. Oct. 8, as before, sitting with curved back. Oct. 15, lying on the floor of the cage, breathing slowly, superficially, dying. Dead in the evening.

The vessels on the surface of the brain rather vividly injected, a marked contrast between the cortex and medulla. The surface of the spinal cord pale. On section the white matter much swollen, the grey matter distinctly marked, of a greyish-red colour with indistinct red spots. Microscopic examination of the spinal cord showed an inconsiderable hyperaemia, no haemorrhages and no cellular infiltration but a considerable hypertrophy of the glia cells, the ganglion cells being, especially in the lumbar region, highly degenerated with a diffusely stained nucleus, the cell body homogeneous, shrunken, deeply stained, intensely vacuolated or fenestrated, and deeply infiltrated by the surrounding large, clear glia cells.

The *intestinal* fluid was filtered through a Heim, and 60 c. c. of the filtrate were, on Sept. 17, intraperitoneally injected into *Macacus cynomolgus* no. 19. Sept. 22, morning: grasps badly; afternoon: lying on the floor of the cage, breathing superficially, is able to hang by the left hand but not with the right. In the evening the animal is very ill and was consequently killed.

The blood vessels on the surface of the spinal cord show up distinctly, the surface on section moist, not swollen, the boundary of the grey matter indistinct. In the cervical enlargement the commissural artery is distinctly marked and the commissure itself of a reddish hue. Microscopic examination shows scattered haemorrhages, some of them quite large, moderate hyperaemia but no cellular infiltration and as a rule no hypertrophy of the glia cells; a great number of the ganglion cells have a quite normal

appearance, a small number being, however, somewhat dark, shrunken, homogeneous and vacuolated, though not to any great extent.

Non-filtered material from the spinal cord of the preceding monkey was, on Sept. 28, intraperitoneally injected into the left sciatic nerve of *Macacus cynomolgus* no. 46. Oct. 14, climbs slowly and is easy to catch. Oct. 15, weak in the fore legs, tumbles and falls face downwards when jumping down to the floor. Oct. 16, runs and climbs very badly, reels and loses its balance both on the fore and hind legs. Oct. 17, dead.

Hyperaemia of the surface of the brain, the cortex in some places being of a deep red colour. The blood vessels of the lumbar cord as well as of the whole of the anterior fissure vividly injected, on section the surface greatly swollen, especially in the cervical region, and moist, the grey matter showing a very marked reddish discoloration. The microscopic examination shows oedema and moderate hyperaemia of the spinal cord, but no haemorrhages and no cellular infiltration; distinct hypertrophy of some of the glia cells; in the medulla oblongata and the entire spinal cord is found an extensive degeneration of the majority of the ganglion cells, which are shrunken, homogeneous, deeply stained, intensely vacuolated and to a high degree infiltrated by the enlarged glia cells, so that only star-like bodies or sponge-like masses are left.

An emulsion was made of 2 grammes of the *spinal cord* from the dead girl, filtered through a Heim and, on Sept. 27, injected into the peritoneal cavity of *Macacus cynomolgus* no. 39. Oct. 2, complete paralysis of both legs. Oct. 3 dead.

The vessels on the surface of the brain moderately distended, the brain otherwise without macroscopical change. The pia of the spinal cord hyperaemic in the lumbar region; on section the spinal cord swells moderately and the grey matter is of a rather pronounced red colour with red spots. Microscopic examination of the spinal cord: Hyperaemia but no large haemorrhages, marked cellular infiltration of the membranes, diffuse and in groups in the substance of the grey matter as well as around the vessels both of the grey and white matter; hypertrophy of some of the glia cells, degeneration and leucocyte-neuronophagia of a great number of the ganglion cells.

Monkey no. 24, injected with the tracheal fluid, was attacked 2½ weeks after the injection and died 9 days later. It presented no distinct paralyses, it is true, but the spinal cord showed such a well marked and diffuse degeneration of the nerve cells, that there can be no doubt as to the diagnosis of poliomyelitis. The monkey no. 19 which was injected with the specimen obtained from the intestine was attacked on the 5:th day and was the same evening found in a dying condition, without showing any signs of isolated paralysis and presenting only small changes in the spinal cord. The control monkey no. 40, on the other hand, got pareses and showed very marked degeneration of the nerve cells. The monkey inoculated with the emulsion of the spinal cord of the dead girl was completely paralyzed in the legs. The spinal cord showed, besides hypertrophy of the glia cells, also cellular infiltration and leucocyte-neuronophagia, which changes were absent in the animals inoculated with the fluids.

#### Case VIII.

*Sigurd G—n*, a boy aged 13, from Upland.

Was attacked simultaneously with a 9-year old brother in the morning of Sept. 9 with general symptoms of fever. The latter died with symptoms of paralysis of the respiratory organs on Sept. 11. Somewhat later in the day of onset signs of pareses of the right arm and right side of the face were observed, the pareses increasing continually during that and the next day. Was admitted to the Epidemic Hospital of Uppsala in the evening of Sept. 11. Lively, wide awake and talkative, paralysis of the right side of the face, slight dysphagia, paresis of the muscles of the neck and back of the head on the right side, paralysis of the right arm, distinct paresis of the left arm, no difficulty in breathing, no paresis of the legs. Sept. 12, morning: the pareses have rapidly increased, paralysis of the respiratory and laryngeal muscles, the left side of the face intact, the



motor power of the legs good. Died in the evening of the same day. Post-mortem examination the following day.

Of the fluid obtained from the *mouth* and *nose*, 20 c. c. were filtered through a Heim and concentrated for some days over  $H_2SO_4$ , the residue being injected into the peritoneal cavity of *Macacus cynomolgus* no. 26, on Sept. 19. Sept. 24, the animal has been sitting for some days with the back curved, seems to day to be very ill, grasps badly, but can hang by the hands; when walking, the legs give way. Sept. 26, dead.

The vessels of the pia of both brain and spinal cord moderately distended with blood, on section the cervical cord swollen, the grey matter of a reddish hue with red spots and streaks; the grey matter of the lumbar cord also of a reddish colour, sections through the medulla oblongata plainly showing fine bloodvessels. Microscopic examination of the spinal cord: Moderate hyperaemia, oedema and solitary haemorrhages, in some places slight signs of perivascular cellular infiltration, but not diffuse; the glia cells generally hypertrophied, a great number of the ganglion cells degenerated, shrunken, homogeneous and deeply stained.

From the spinal cord of the preceding monkey an emulsion was made, and, on Sept. 29, intraneurally inoculated, into the left sciatic nerve of two *Macaci cynomolgi*, nos. 47 and 48.

No. 47. Oct. 18, paretic in both fore legs, falls on the nose when running. Oct. 20, jumps about on the hind legs, paralytic in the arms. Oct. 28, dead.

The pia mater of the brain hyperaemic, the cortex partially rather red. The vessels of the spinal cord only slightly perceptible, in the cervical and lumbar cords no macroscopic changes observed, but in the dorsal region the grey matter is somewhat reddish. Microscopic examination: Neither hyperaemia, haemorrhages nor cellular infiltration in the spinal cord; some of the glia cells enlarged, clear, transparent; the ganglion cells in some places well preserved, showing a plain tigroid substance, in others, again they are homogeneous and vacuolated, though not to any higher degree.

No. 48. Oct. 2, paretic in both arms, often falling towards the right. Oct. 9, has grown much worse to-day, lies almost motionless on the floor of the cage, breathing superficially. Died at noon.

The brain shows no macroscopic changes. The pia of the spinal cord moderately hyperaemic in the cervical and lumbar regions, on section here very marked swelling, the grey matter



rising above the surface, its colour reddish with red spots. Microscopic examination: Moderate hyperaemia of the grey matter and considerable oedema, but no haemorrhages nor any cellular infiltration; considerable hypertrophy of the glia cells and intense degeneration of most of the ganglion cells which are shrunken, deeply stained, homogeneous, vacuolated and extensively attacked by the surrounding large, clear glia cells, in several places only small, dark remnants of the nerve cells left.

The *intestinal* fluid, 60 cc. was filtered through a Heim and injected intraperitoneally into *Macacus cynomolgus* no. 20, on Sept. 17. Was found dead the following day. The post-mortem examination revealed septic peritonitis.

About 2 grammes of the *spinal cord* of the dead boy were emulsified and, after filtration injected into the peritoneal cavity of *Macacus cynomolgus* no. 40, on Sept. 27. Oct. 5, runs badly, sometimes falling forwards and to the left. Oct. 6, climbs very badly, runs joggingly and falls on its nose. Oct. 11, parietic in both hind legs, especially the right. Oct. 13, lies motionless on the floor of the cage, dying. Oct. 14, dead.

The vessels on the surface of the brain very distended and the cortex reddish. The vessels of the lumbar cord rather much distended with blood, the section here swollen and the grey matter distinctly reddish discoloured with red spots and streaks; the same appearance, though less distinct, is observed in the cervical region of the cord. Microscopic examination of the cord shows hyperaemia and oedema but no cellular infiltration; considerable enlargement of most of the glia cells; the greater part of the ganglion cells show signs of disintegration or else intense degeneration, are shrunken, deeply stained, highly vacuolated and encroached upon by the enlarged glia cells, so that often only a small star-like body or a sponge-like net-work remains. The changes are most pronounced in the lumbar region and in the medulla oblongata.

☐ Monkey no. 26 which had been infected with the specimen obtained from the mouth, did not, it is true, present any typical paralyses, but the spinal cord showed degeneration of the nerve cells, and an emulsion of the same caused after injection distinct paralyses in both of the control-monkeys, the spinal cord of one

of the animals showing to a large extent a considerable degree of degeneration of the ganglion cells. An emulsion of the spinal cord of the dead boy produced distinct pareses in the injected monkey after about 8 days of incubation, the animal dying about a week later. In the spinal cord were found neither cellular infiltration nor leucocyte-neuronophagias, but a very marked degeneration of the nerve cells and a great enlargement of the glia cells.

#### Case IX.

*Gustaf Erik G—n*, a labourer, 35 years of age, from Stockholm.

Was taken ill on Sept. 14 after having suffered from headache for about six days and having been unable to go to work for one week; is said to have been weak in the legs and stated himself that he had seen double. Has not associated with anyone attacked by illness. Sept. 15, worse, vomiting also setting in.

Was admitted to the Epidemic Hospital of Stockholm on Sept. 16. Looks drowsy but is fully conscious and clear in his mind, no stiffness nor any tenderness of the neck, complains of frontal headache, nothing from the cranial nerves, fair strength in the arms, is able to stand but falls easily on account of weakness of the legs, can get into bed himself and lie down. The petallar reflexes increased. Sept. 17, much worse than yesterday evening, distinct facial paresis of the left side, movements of palate and eyes normal, swallows well, no nystagmus, can easily sit up and lie down, power of the abdominal muscles good, movements of the arms uncertain, the bladder reaches to the umbilicus, the urine passed in the bed during the night. In the evening very drowsy, sensorium, however, free, replies when spoken to and obeys when commanded, has had a few attacks of vomiting to-day, does not complain of any pains, but is tender when knocked on the left side of the head in the temporal region. Sept. 18, the condition has grown considerably worse during the night, is now perfectly unconscious, the respiration chiefly costal, irregular, frequency 16, pale and cyanotic, perspires. Died in the afternoon. Post-mortem examination on Sept. 19.

Specimen obtained from the *mouth*, *pharynx* and *nose*. After filtering through a Heim, 60 c. c. were, on Sept. 24, injected into the peritoneal cavity and 1 c. c. into the left sciatic nerve of *Macacus cynomolgus* no. 31. Oct. 6, runs strikingly slowly and badly, climbs badly, on jumping down the forelegs sometimes give way, the animal falling on its nose. Oct. 12, as before. Oct. 14, very bad, thin, back crooked, climbs very slowly, does not run, walks slowly and with uncertainty, is easy to push over. Oct. 15, dead.

The blood vessels on the surface of the brain moderately filled, the cerebral cortex here and there reddish. The vessels of the spinal cord distinctly visible in the lumbar region, on section the spinal cord everywhere rather markedly swollen and moist, the grey matter distinctly reddish and mottled with red, chiefly in the lumbar cord. Microscopic examination shows hyperaemia, considerable oedema in the lumbar region, no haemorrhages, marked hypertrophy of the glia cells, in the medulla oblongata as well as in the whole of the spinal cord, though chiefly in the lumbar region; considerable degeneration of the ganglion cells which either are completely destroyed or else shrunken, deeply stained, homogeneous, extensively vacuolated and attacked by the surrounding, enlarged glia cells.

The *tracheal* specimen. After filtration through a Heim, 22 c. c. were intraperitoneally, and 1 c. c. intraneurally injected into *Macacus cynomolgus* no. 32, on Sept. 24. Was observed for several months but showed no symptoms of paralysis.

The specimen from the *ileum*. After filtration through a Heim, 50 c. c. of the filtrate were injected into the abdominal cavity, and 1 c. c. into one sciatic nerve of *Macacus cynomolgus* no. 30, on Sept. 24. Nov. 30, climbs somewhat slowly and with jerks. Dec. 4, lies on the bottom of the cage and moves but little, if placed on the floor, the feet give way and the animal makes no attempts to walk, does not climb either, but can hang by the arms. Dec. 5, dead.

The meninges only slightly injected. Some injection over the enlargements of the spinal cord, especially on the dorsal surface, the section of the spinal cord swollen, only slight contrast between the medulla and the cortex, the grey matter distinctly of a light greyish-red colour in all parts of the spinal cord. Microscopic examination: Hyperaemia and solitary haemorrhages but no cellular infiltration, a great part of the glia cells large, clear and transparent; the

ganglion cells degenerated or entirely destroyed in a manner resembling that found in the spinal cord of monkey no. 40.

An emulsion of the *spinal cord* of the dead man was made and after filtration through a Heim 20 c. c. injected into the peritoneum, and 1 c. c. intraneurally into *Macacus cynomolgus* no. 33, on Sept. 25. Oct. 16, climbs less lively, runs joggingly and with some slight degree of ataxia, is easy to catch. Oct. 17, walks slowly, carefully, unsteadily, swaying from one side to the other with the body when sitting, climbs very slowly, can hold on with the hands. Oct. 18, the position of the left hand typical of radial paresis, when walking inclined to fall to the left. Nov. 19, weak, especially in the left arm, the left hand still in the position of radial paresis, weak also in the hind legs, gait unsteady and swaying. Oct. 20, found dead.

The vessels on the surface of the brain markedly injected, the contrast between medulla and cortex being sharp. The surface of the spinal cord pale, on section the grey matter swollen and greyish-red discoloured. On microscopic examination the spinal cord shows a moderate degree of hyperaemia, but neither haemorrhages nor cellular infiltration; no leucocyte-neuronophagias, but considerable hypertrophy of the glia cells and a marked degree of degeneration of the nerve cells of about the same appearance as in the spinal cords of the two above mentioned dead monkeys.

Only the monkey infected with the emulsion of the spinal cord developed a pretty distinct, isolated paresis, all the others showed only general weakness of the muscles. In all of them hypertrophy of the glia cells and very pronounced degeneration of the nerve cells were found, but on the other hand there were no signs at all of any cellular infiltration nor of leucocyte-neuronophagia, not even in the animal infected with the emulsion of the spinal cord.

#### Case X.

*Artur Valdemar C—n*, a boy of 14, Värmdö.

Onset on Sept. 16 with headache at the top of the head and pains in the back and neck when moving; no vomiting but constipation and a slight cough. During the night of Sept. 18 he observed weakness in the legs.



Was admitted to the Epidemic Hospital of Stockholm on Sept. 18. The general condition rather good, but some stiffness of the neck is ascertained, and the patient experiences pain when moving the head, which falls backwards when he is raised up; the right triceps muscle weak, the left stronger, the left leg can be drawn up, and the knee-joint extended to a certain small degree, and he is also able to move the joints of the left foot and toes a little, but the right leg is, with the exception of the toes, almost completely paralyzed. The triceps reflexes lively on the left side, somewhat weak on the right, the radial reflexes increased, the abdominal, cremaster and patellar reflexes absent, Babinsky distinct on the left, indistinct on the right side. Sept. 19, respiratory paralysis, breathes chiefly with the diaphragm, died in the afternoon. Post-mortem examination on Sept. 20.

Fluid obtained by washing *the mouth, nose and pharynx*. After filtering through a Heim, 60 c. c. were injected into the peritoneal cavity, and 1 c. c. intraneurally into the left sciatic nerve of *Macacus cynomolgus* no. 29, on Sept. 24. Sept. 27, does not run as quickly as usually. Oct. 6, paralyzed in both hind legs, most completely in the left, trembling in the left arm and hand, is able to rise, but cannot walk. Oct. 7, dead.

The vessels on the surface of the brain moderately congested, the cortex in some places reddish, the section very moist. The vessels on the surface of the spinal cord appear very indistinctly, on section the spinal cord swells inconsiderably, is somewhat moist and the grey matter spotted with red. Microscopic examination of the spinal cord: Hyperaemia, haemorrhages and oedema, accumulation of leucocytes in the vessels, cellular infiltration of the pia, diffuse, group-like and perivascular cellular infiltration in the spinal cord, hypertrophy of some of the glia cells, intense degeneration and very marked acute neuronophagia of the ganglion cells.

Fluid obtained from the *trachea*. The specimen having been kept for four days in a vacuum over  $\text{H}_2\text{SO}_4$  for concentration, it was filtered through a Heim, and 45 c. c. of it injected into the peritoneum, and 1 c. c. into the left sciatic nerve of *Macacus cynomolgus* no. 28, on Sept. 9. Sept. 27, moves less lively, has some difficulty in climbing, seems weaker, but shows no distinct paresis. Sept. 29, about the same as before. Oct. 6, climbs with difficulty, runs joggingly, keeping the body straight and motionless. Oct. 8, as before, back crooked and gait swaying. Oct. 13, is lying almost motionless



on the bottom of the cage, breathing slowly, superficially. Oct. 14, dead.

The brain without macroscopical change. No distinct hyperaemia of the spinal cord, in both the lumbar and cervical regions the cord on section somewhat swollen, moist and the grey matter distinctly reddishly discoloured. Microscopic examination: No noticeable hyperaemia, no haemorrhages and no cellular infiltration, but moderate oedema, considerable enlargement of the glia cells, which are clear and transparent; the nerve-cells of the spinal cord and the medulla oblongata highly degenerated, shrunken, homogeneous, deeply stained, vacuolated and greatly encroached upon by the hypertrophic glia cells; sometimes there remain of the ganglion cells only small, deeply stained, ragged masses.

The specimen from the *ileum*. After filtration through a Heim, 40 c. c. of the fluid were injected into the peritoneal cavity, and 1 c. c. into the left sciatic nerve of *Macacus cynomolgus* no. 27, on Sept. 24. Sept. 30, climbs and crawls strikingly bad, is evidently paretic in all the extremities, though not in a high degree, cannot rise on its legs, falls now and then, can hardly hold up its head, the upper eyelids have fallen down, and there is complete loss of the mimic movements of the face. In the afternoon paralysis of the muscles of the neck. Oct. 1, is to-day lying almost motionless on the floor of the cage, breathing superficially. Oct. 2, dead.

The vessels on the surface of the brain are rather distended, the cortex of the brain moist, in some spots reddish. The dura mater and the extradural tissue hyperaemic, the blood-vessels on the surface of the spinal cord distinctly injected only in the lumbar region, the section of the spinal cord moderately swollen, moist, the grey matter distinctly, reddishly discoloured, showing red spots and streaks. Microscopic examination of the spinal cord: Inconsiderable cellular infiltration of the pia, marked hyperaemia and numerous haemorrhages in the grey matter, accumulation of white corpuscles in the vessels, cellular infiltration in larger and smaller groups and around the vessels, the glia cells generally hypertrophic; the greater part of the ganglion cells degenerated, shrunken, star-shaped, some deeply stained and others pale, karyolysis and pyknosis, the degenerated ganglion cells being often attacked by much enlarged glia cells.

Of the *spinal cord* of the deceased boy an emulsion was made

and filtered through a Heim filter, whereof 20 c. c. were injected into the peritoneal cavity, and 1 c. c. into the left sciatic nerve of *Macacus cynomolgus* no. 34, on Sept. 25. On Sept. 30, less lively, runs with a limp and slowly, climbs rather well, although somewhat slowly, the left arm being weaker. Oct. 2, paresis of the left hand (radial paresis-position), walks joggingly, climbs badly. Oct. 6, death.

The vessels of the brain rather distended, especially at the base, the superficial vessels of the spinal cord less congested. On section the cervical cord is swollen, the grey matter showing a distinct but light reddish-grey discolouration, in the lumbar region the changes are less marked. Microscopic examination shows considerable hyperaemia and haemorrhages in the spinal cord, but no quite definite cellular infiltration, no hypertrophy of the glia cells, nor any degeneration of the nerve cells as in the monkeys nos. 27 and 28.

All the animals used at this experiment were attacked after a relatively short period of incubation, 3—6 days, and died after 1—17 days illness. Three of them showed marked pareses, also the one infected with the intestinal specimen, which developed facial paresis and paralysis of the muscles of the neck. Nevertheless the histological changes found in the spinal cords of these animals differed greatly. One, the monkey infected with the buccal fluid showed cellular infiltration as well as leucocyte-neuronophagia; the other, infected with the fluid from the intestine, showed cellular infiltration, but no leucocyte-neuronophagia, the nerve cells showing degeneration and glia-cell-neuronophagias; and lastly in the monkey infected with the emulsion of the spinal cord, cellular infiltration as well as leucocyte-neuronophagia were totally absent while the degeneration of the nerve cells and the enlargement of the glia cells were rather considerable. The monkey infected with the tracheal fluid showed similar changes.

## Case XI.

*Rolf B—m*, 2 years old, from Jonsered.

Onset on Sept. 16 with a general feeling of malaise and vomiting. On Sept. 19 the mother noticed, that the boy could not stand on his legs. On Sept. 21, he could not move his left arm and was then sent to the Epidemic Hospital of Gothenburg. There it was ascertained that he had paresis of the arms and legs, as well as of the muscles of the head, the greater number of the groups of muscles in question being completely paralyzed. The patellar reflexes were absent. Sept. 24, during the night a rapid change for the worse with regard to his general condition, the muscles became flaccid and the pulse could not be felt, died in the morning. Post-mortem examination on the same day.

The fluid obtained by washing the *mouth*, *nose* and *pharynx* was filtered through a Heim filter, and 30 c. c. injected intraperitoneally, and 1 c. c. intraneurally into the left sciatic nerve of *Macacus cynomolgus* no. 36, on Sept. 26. Oct. 17, does not climb as rapidly as before, the movements of the legs on running not quite natural, is easy to catch. Oct. 21, weak in the right arm. Oct. 22, almost complete paralysis of all the extremities, lies on the bottom of the cage and cannot rise. Oct. 23, moves only slightly, dying; killed.

The meningeal vessels hyperaemic, the cortex partly greyish-red. The vessels of the anterior surface of the spinal cord injected, on section the spinal cord not swollen but a little moist, the grey matter reddish throughout the whole of the cord. Microscopic examination shows inconsiderable hyperaemia, no haemorrhages, and no cellular infiltration, but hypertrophy of some of the glia cells and degeneration of the nerve cells, which in the medulla oblongata are to a large extent either pale, finely granular, almost dissolved or else shrunken, deeply stained, homogeneous and vacuolated, some of them being more or less deeply invaded by enlarged glia cells; in the spinal cord the ganglion cells are considerably less changed, a great many showing distinct tigroid substance, others, on the other hand, being somewhat shrunken, deeply stained and homogeneous.

The *tracheal* fluid was filtered through a Heim filter, and, on Sept. 27, 15 c. c. there were injected intraperitoneally, and 1 c. c. intraneurally into the left sciatic nerve of *Macacus cynomolgus* no. 37.

Oct. 2, runs slowly, not naturally, is easy to catch, weak in both hands. Oct. 5, for some days the animal holds the hind legs close together when running. Oct. 6, lying almost motionless on the bottom of the cage. Died in the evening.

The brain and its membranes show no macroscopical change. Corresponding to the medulla oblongata and the lumbar portion of the cord, the pia is moderately hyperaemic, on section the cord considerably swollen, in the lumbar region almost in a state of dissolution, the grey matter indistinct. Microscopic examination: Inconsiderable hyperaemia, no haemorrhages and no cellular infiltration but much oedema; great hypertrophy of the glia cells and considerable degeneration of the nerve cells, these latter being shrunken, deeply stained, intensely vacuolated and encroached upon by the surrounding enlarged glia cells.

The fluid obtained from the *ileum* was filtered through a Heim and, on Sept. 26, injected into *Macacus cynomolgus* no. 35, 30 c. c. intraperitoneally and 0.5 c. c. intraneurally. The animal died on Sept. 28 of acute peritonitis rich in bacteria.

The monkey infected with the fluid from the mouth was attacked after 21 days and the one infected with the tracheal fluid after a period of incubation of 5 days. Both died after a brief illness, lasting 4—6 days, with symptoms of progressive general weakness of the muscles but without having presented any distinct, isolated pareses. In both a considerable destruction of the nerve cells of the spinal cord and of the medulla oblongata was found, but no cellular infiltrations nor any leucocyte-neuronophagias.

## Case XII.

*Per L. J. L—n*, a boy aged 13, Mariefred.

Was unwell with vomiting and headache on Sept. 18, but nevertheless he went to school. In the evening he was taken ill with bleeding from the nose, vomiting and a severe headache. On Sept. 24, temp. 39.8° C., very drowsy, repeated vomitings, nystagmus, slight signs of strabismus, no double images, no stiffness of the neck. Was admitted to the Epidemic Hospital of Mariefred.



In the afternoon the temperature was  $40.4^{\circ}\text{C}$ ., pulse 144, wandering in his mind, stiff in the neck, incessant vomiting, free salivation, no diarrhoea, increased nystagmus, widely dilated pupils, when he is clearer in his mind he has double vision, paresis of the left facial nerve, often spasmodic grimaces of the right side of the face, the respiration undisturbed, but some difficulty in coughing, no pareses of the extremities, no tenderness over the spine, can pass his water, the patellar reflexes normal. Died in the morning of Sept. 26. Post-mortem examination the same day.

Fluid obtained by washing the *mouth*, *nose* and *pharynx*. After filtration through a Heim 25 c. c. were injected into the peritoneal cavity and 1 c. c. into the left sciatic nerve of *Cynocephalus hamadryas* no. 43, on Sept. 28. The animal remained well.

The fluid obtained from the *ileum* was intraperitoneally and intraneurally injected into *Cynocephalus hamadryas* no. 41, on Sept. 28, without producing any symptoms of disease.

Of 1 gramme of the *spinal cord* of the dead boy an emulsion was made with saline solution and after filtration through a Heim injected, intraperitoneally and intraneurally, into *Cynocephalus hamadryas* no. 42, on Sept. 28. Oct. 28, climbs slowly and is generally rather slow in its movements, weak in the hind legs, when walking keeping them flexed at the hip-joints and being unable to rise on them. Oct. 31, dead.

The vessels on the surface of the brain and spinal cord vividly injected, the section of the spinal cord swollen, rather a marked contrast noticeable between medulla and cortex, the grey matter everywhere of a reddish hue. Microscopic examination: Pronounced hyperaemia, haemorrhages, sometimes rather large, and oedema, but no cellular infiltration; considerable hypertrophy of the glia cells and degeneration of the nerve cells. These latter are deeply stained, much shrunken and vacuolated, often leaving only small, irregular, radiating bodies, or else they are pale, finely granular, as if dissolved. The changes are especially marked in the medulla oblongata.

The injected fluid from the mouth and intestine did not in this case produce any perceptible symptoms of disease in the monkeys. The monkey which had been infected with the emulsion of the spinal cord of the dead boy was, on the other hand, taken



ill after a period of incubation of one month and died three days later showing the picture of general muscular weakness but no signs of any isolated, distinct pareses. The spinal cord showed a high degree of degeneration of the ganglion cells but no cellular infiltration, nor any leucocyte-neuronophagia.

### Case XIII.

*Nils V. L—n*, a boy of six and a half years from the parish of Rö.

Was attacked, on Sept. 22, with fever and tenderness over the back of the head. On Sept. 24. condition worse, temp. 40° C., apathetic, complained of tenderness in the body and of headache. Sept. 26, the left upper extremity paralysed, of the right arm only the fingers can be moved. The breathing difficult, chiefly abdominal. Died on the 27.; post-mortem examination the same day.

The fluid obtained by washing the *ileum*. After filtration through a Heim, 2,5 c. c. were, on Sept. 28, injected into the peritoneal cavity and 1 c. c. intraneurally into the left sciatic nerve of *Cyncephalus hamadryas* no. 44.

Oct. 5, both hands in the typical position of radial paralysis, walks on the knuckles, does not catch with the hands, is unable to take an apple with them, instead of which the animal bends forwards taking it directly with the teeth, mostly sitting on the floor of the cage, keeping the arms still and limp. Oct. 6, is able to move better to-day, catches about normally, and can take an apple with both hands and put it to the mouth. Recovered completely.

Although the monkey inoculated with the intestinal specimen did not die, but recovered completely after rather a short illness, it seems nevertheless quite right to regard the illness as poliomyelitis, as the animal showed quite distinct pareses, appearing at the lapse of about the usual period of incubation, characteristic of poliomyelitis in monkeys.

## Case XIV.

*Lilly G—n*, 9 years old, from Jönköping.

Was attacked on Sept. 21 with fever and headache, but did not take to the bed before Sept. 23. Was admitted to the Epidemic Hospital of Jönköping on Sept. 25. On arrival, she had 39,7° C., headache, pains in the back and stiffness of the neck, but no pareses. Sept. 26, weakness of the back, difficulty in rising in bed. Sept. 27, pains in both legs, weakness in the left leg with marked peroneal paresis, distinct pareses of the deltoid muscles. Sept. 28, pareses in the legs and arms, in the latter especially ulnar paresis, difficulty in speaking, the tongue refusing to obey, some difficulty in swallowing, paresis of the intercostal muscles, the chest not moving with respiration. Died in the morning of Sept. 29. Post-mortem examination the same day.

The fluid obtained by washing the *mouth*, *nose* and *pharynx* was first filtered through a Heim, and then refiltered through a Berkefeld filter. Of the filtrate 60 c. c. were injected intraperitoneally and 0,5 c. c. intraneurally into *Macacus rhesus* no. 51, on Sept. 30. The monkey developed no symptoms of disease.

Fluid obtained from the *trachea*. After filtration through a Heim filter, 45 c. c. were injected into the peritoneal cavity, and 0,5 c. c. intraneurally into the left sciatic nerve of *Cynocephalus hamadryas* no. 50, on Sept. 30. Oct. 4, holds the left hand in the position of radial paresis and walks on the wrist. Oct. 5, runs livelier to day but climbs somewhat slowly, no distinct paresis-position. Oct. 8, runs badly, limps in the left leg, is easy to catch. Oct. 16, looks ill, is swollen in the face, runs and climbs badly, but has no distinct paresis. Oct. 17, worse, trembles all over the body, when offered an apple the animal takes it very carefully, clumsily, finding it difficult to retain. Oct. 18, is sitting still, does not rise on the hind legs, is easily pushed over and then finds it difficult to rise again. Later on in the day, it trembles and shakes all over, when attempting to rise, drags itself along, falls easily on the left hind leg which is distinctly paretic; the oedema of the face has disappeared. Oct. 19, is lying on the bottom of the cage, moving only slightly; is killed.

The surface of the brain vividly injected, that of the spinal cord paler, rather a marked contrast between the cerebral cortex and the medulla; the section of the spinal cord not swollen but moist, the

grey matter distinctly marked, somewhat red in colour. Microscopic examination: No cellular infiltration, no oedema; hypertrophy of a small number of the glia cells, considerable degeneration of the nerve cells in the medulla oblongata, less pronounced in the spinal cord. The changes are very much the same as those found in the spinal cord of monkey no. 42.

Specimen from the *ileum*. First filtered through a Heim filter and then through a Berkefeld. 45 c. c. of the filtrate were, on Sept. 30, injected intraperitoneally, and 0.5 c. c. intraneurally into Baboon no. 49. Oct. 8, does not move willingly, climbs badly and is easy to catch, no distinct paresis. The monkey recovered after a few days and no further changes were noticed during the period of observation which lasted several months.

An emulsion with saline solution was made of the *spinal cord* of the dead girl, filtered through a Heim and, on Oct. 1, injected into *Cynocephalus hamadryas* no. 54, 40 c. c. intraperitoneally, and 1.0 c. c. into the left sciatic nerve. Oct. 3, climbs slowly, somewhat weak especially in the left hand. Oct. 4, dead.

The vessels on the entire surface of the brain markedly injected, the cortex a light greyish-red. The upper dorsal region showed small epidural haemorrhages, slight injection of the vessels on the surface of the spinal cord, on section the spinal cord is slightly swollen, the surface moist, the grey matter discoloured a greyish-red with solitary red spots and streaks. Microscopic examination: Hyperaemia and rather numerous haemorrhages but no cellular infiltration, distinct hypertrophy of some of the glia cells; considerable degeneration of most of the ganglion cells, which are either pale, finely granular with almost liquified edges, or else, which is the more common change, they are shrunken, deeply stained, homogeneous, highly vacuolated and deeply notched by the large, clear, surrounding glia cells. The nuclei of the ganglion cells are either fairly normal or else shrunken, diffusely and deeply stained.

The fluid obtained by washing the mouth produced no perceptible symptoms of disease in the animal used for the experiment. The animal which had been inoculated with the fluid from the trachea was attacked four days later, showed tremor and distinct paresis of one of the hind legs, and died after 14 days' illness. The

medulla oblongata especially showed considerable degenerative changes in the ganglion cells but neither cellular infiltration nor leucocyte-neuronophagia. That this was a case of experimental poliomyelitis there seems, however, no reason to doubt. In all probability the Baboon which had been infected with the intestinal fluid, has also had a slight attack of the disease. The monkey infected with the emulsion of the spinal cord of the dead girl, was attacked on the second day and died on the following day, without presenting any signs of a fully distinct paresis. The spinal cord showed no cellular infiltration nor any leucocyte-neuronophagias, but an advanced degeneration of the ganglion cells.

\*       \*       \*

As will appear from the accounts of the microscopic examinations, in several cases which we have regarded as positive, we have not found those changes which have hitherto been considered as the most characteristic of the acute poliomyelitis, i. e. cellular infiltration, diffuse, in groups or perivascular and neuronophagia with the ganglion cells full of mononuclear and polymorphonuclear leucocytes. Instead we have observed a *characteristic change in the cells of the supporting tissue* which were found to be enlarged, without any distinct processes, clear and transparent. Also we have found a considerable *degeneration of the ganglion cells*, into which the large, clear, surrounding glia cells, though usually not in any great numbers, have eaten their way, so to speak, thus causing large excavations in the degenerated ganglion cell and often reducing this to a small, dark mass or a star-shaped body, presenting a sharp contrast to the clear, transparent glia cells. *We*



*consider these changes also to be due to, and to a certain degree to be characteristic of the effect of the virus of infantile paralysis.* That such really is the case, is evident firstly from the fact that the clinical symptoms were characteristic of poliomyelitis in several of the cases in which only the above mentioned changes were observed. Further, the monkey no. 27 which had been infected with the intestinal fluid from case X, showed very characteristic perivascular infiltrations, but no neuronophagias with invasion of polyblasts and polymorphonuclear leucocytes, the ganglion cells only being degenerated and deeply excavated by the large, clear surrounding cells (Fig. 2). The spinal cord from the monkey no. 22 which was infected with the tracheal fluid from case III, showed, besides haemorrhages, no other changes than hypertrophy of the cells of the supporting tissue together with the changes in the ganglion cells just mentioned (Fig. 3). The control monkeys nos. 55 (Fig. 4) and 56 which had been inoculated with this spinal cord, showed on the other hand, quite typical perivascular infiltrations and leucocyte-neuronophagias with a free invasion of leucocytes into the ganglion cells. Moreover, the monkeys which have been inoculated with emulsions of the spinal cords obtained from cases of infantile paralysis have several times only shown similar degenerative changes and this even when, as in case no. X, the specimens obtained by washing have caused infiltrations and leucocyte-neuronophagias in the spinal cords of the other inoculated monkeys. We shall discuss this matter in detail later on.

The following table gives a resumé of the results obtained in the foregoing investigations. The monkeys



dying from secondary infection are not included in the series.

Table I.

		Mouth	Trachea	Intestine	Spinal cord
18	Oskar G. E. A—n	0	+	+	—
14	Gunnar S—t	75	0	+	+
6	Gustaf Adolf H. V—n	3	+ < + +	+?	—
2	Carl Runo C—n	5	+	+	+
11	Siri Linnea E—n	4	—	+	—
4	Einar L—l	9	+	—	+
8	Jenny Florida F—n	6	+	+	+
13	Sigurd G—n	2	+ < + +	—	+
3	Gustaf Erik G—n	4	+	0	+
14	Artur Valdemar C—n	2	+	+	+
2	Rolf B—m	8	+	—	—
13	Per Lars J. L—n	8	0	0	+
6	Nils V. L—n	5	—	+	—
4	Lilly G—n	8	0	+	+
		11	10	11	9

Only in the case of one person have we been unsuccessful in demonstrating the presence of the microbe of infantile paralysis in any of the fluids obtained by washing. Out of 11 specimens from the mouth a positive result has been obtained in 7, and a negative in 3 cases; in one case the result was uncertain. Of 10 specimens from the trachea the presence of the microbe was successfully demonstrated in 8. The 11 intestinal specimens gave 8 positive, one negative and 2 uncertain results. *Considering all these facts together, the total number fluids examined being 32, a sure and positive result has been obtained in 25 (= 78 %).* The injected emulsion of the spinal cords of the persons examined has in every case produced poliomyelitis in

the inoculated monkeys, only one of these surviving the infection but with permanent complete paralysis of one arm.

## 2) Investigations on living persons.

The result of the investigations made on dead bodies must be considered as highly satisfactory and has induced us to proceed without delay to investigate the secretion from the mucous membranes of living persons attacked by infantile paralysis. To obtain tracheal secretion from a living person is extremely difficult, and for that reason we have abstained from an investigation of this and been content with the examination of the material obtained from the *mouth*, *nose* and *pharynx*, as also the *large intestine*. The specimens from the nasal and buccal cavities were obtained either by injecting fluid into the nose and allowing it to pass out through the mouth, or by irrigation with a common pharyngeal syringe, which was introduced so far that the pharynx was washed also. The patient has also been made to gargle when this was possible. The specimen from the intestine was obtained in the following manner. The intestinal contents having been cleared out by means of an ordinary enema, the intestine was after a little while thoroughly irrigated, an intestinal tube being passed as far as possible into the sigmoid flexure and the injected fluid allowed to run in and out repeatedly through the tube. As a rule the fluid thus obtained contained only very little faecal matter. All the irrigations were done with physiological saline solution and the quantity so regulated that the specimen obtained amounted to, at the most, about 150 c. c.

The specimens thus obtained were filtered through a Heim filter and then injected into the peritoneal cavity and into one of the sciatic nerves of monkeys. The quantity of fluid introduced into the peritoneal cavity is recorded in each case. The quantity injected into the nerve was generally 1—2 c. c. in a few cases 2.5 c. c. As in the preceding investigations, each specimen fluid was as a rule injected into one monkey only. When the clinical symptoms have been characteristic of acute poliomyelitis, we have contented ourselves with a microscopic examination of the spinal cords of the dead monkeys. If, on the other hand, the animals died suddenly, or after an illness showing only few characteristics, we have in addition made control inoculations with the spinal cord of the animal in question.

#### Case XV.

*Gunhild G—n*, a girl aged 6, from Edhult parish.

Onset Sept. 7 with fever, headache, ravings and hallucinations, vomiting, constipation and stiffness of the neck and back. Sept. 9, the temperature 39.2° C., paresis of the left leg. General condition worse. The patient died on Sept. 11.

The specimen from the mouth and nose was obtained on Sept. 9.

40 c. c. of the fluid from the *mouth* was, on Sept. 19, injected into the peritoneal cavity of *Macacus cynomolgus* no. 25. Oct. 13, in the morning, poor, lying on one side but being able to move a little. In the evening the animal is very ill, does not move and experiences difficulty in breathing. Oct. 14, dead.

A moderate hyperaemia of the surface of the brain, the cortex here and there of a reddish hue. The vessels on the surface of the spinal cord corresponding to the lumbar portion are plainly visible, the section is swollen, especially in the lumbar region, moist, the grey matter shows a distinct reddish discoloration with red spots and streaks.

The microscopic examination shows a marked hyperaemia and

rather numerous haemorrhages, but no distinct cellular infiltrations, though in some places the nearest surroundings of some of the smaller vessels appear rather rich in cells; hypertrophy of some of the glia cells; degeneration of a great number of the nerve cells, both in the medulla oblongata and in the spinal cord, the latter being either very pale, finely granular or else shrunken, dark, homogeneous and highly vacuolated, and often deeply infiltrated by the surrounding large, clear cells.

The monkey used for this experiment, was found, 24 days after inoculation with the buccal specimen, in a condition of general paralysis. It grew rapidly worse and died with symptoms of respiratory failure. The microscopical examination of the spinal cord proves without doubt the presence of experimental poliomyelitis, the disease having run a speedy course after a relatively long period of incubation.

#### Case XVI.

*Ingrid S—g*, a girl aged 5, from Stockholm.

Two other children of the same family attacked by poliomyelitis. She was admitted to the Epidemic Hospital of Stockholm on Sept. 27.

The general condition very bad, some stiffness of the neck and pains in the back on bending the head forwards; the right pupil somewhat larger than the left one, the movements of the eyes normal, the lower branch of the right facial nerve paretic; she walks perhaps a little uncertain but moves the arms normally. The triceps, abdominal and plantar reflexes lively, the patellar reflexes absent, Babinsky positive on both feet, the urine is passed in bed. Sept. 28, the stiffness of the neck persists, more apathetic than yesterday, the tongue deviates to the right on being extended, and the speech is very slurred. Sept. 29, very drowsy, is, however, able to understand what is said to her, and replies when addressed, still stiff in the neck, large-sized tracheal râles are heard. She apparently has not sufficient strength to cough up the excretion. Oct. 2, has to-day vomited several times, mental state clearer and her answers are lucid. Oct. 11, the general condition has during the

past week continued to improve, the power of the arms and legs is good though her gait is still somewhat staggering, the right facial nerve is still markedly paretic, the reflexes lively. Oct. 30, the facial nerve still very paretic, she cannot close the right eye completely, and the mouth is drawn towards the left, the motor power of the arms and legs call for no remark, the gait normal, the patellar reflexes increased, the triceps reflexes normal. Is discharged on November 1.

The washing of the mouth, nose, pharynx, and intestine was done on Sept. 30.

The specimen from the *mouth*, to the quantity of 60 c. c., was injected, on Oct. 1, into *Macacus cynomolgus* no. 52. Oct. 8, died this morning. Yesterday nothing unusual was observed.

The vessels on the surface of the brain moderately distended, the cortex of a reddish hue. The vessels of the spinal cord are distinctly visible only in the cervical and the lumbar regions. On section the cervical cord is swollen, moist, the grey matter is of a pronounced red colour with numerous red spots and streaks. Similar, though less marked changes are also observed in the dorsal and the lumbar parts of cord. Microscopic examination: Slight cellular infiltration in the dura mater, moderate infiltration in the pia and around the vessels in the anterior fissure, hyperaemia and haemorrhages in the spinal cord, and rather marked cellular infiltration in the grey matter, partly diffuse and partly in large groups; hypertrophy of some of the glia cells; the majority of the ganglion cells of the cervical cord degenerated, some of the cells being freely invaded by leucocytes, others shrunken, deeply stained and notched by hypertrophic glia cells; also in the lumbar cord signs of leucocyte-neuronophagias but here a good deal of the ganglion cells are, on the other hand, well preserved.

With a non-filtered emulsion of the spinal cord three other *Macaci cynomolgi*, nos. 67, 68 and 69, were inoculated into one sciatic nerve, on Oct. 9.

No. 67. Oct. 13, weak in the left hind leg. Oct. 14, lying on the bottom of the cage, moves only very little, breathes slowly, superficially and irregularly. Oct. 15, dead.

Rather vivid injection of the vessels at the base of the brain and some injection of the vessels of the cervical enlargement. On section the cord in the cervical region is swollen and the grey matter



of greyish-red colour with fine, red spots. Similar changes in the lumbar enlargement, though less marked. Microscopic examination: Slight infiltration of the pia, hyperaemia and haemorrhages in the spinal cord, marked cellular infiltration around the vessels and in the grey matter, also diffuse and in groups, some of the glia cells being large and clear; some of the ganglion cells are rather well preserved showing distinct tigroid substance, but a large number of them are shrunken, deeply stained, homogeneous and sometimes notched by the surrounding enlarged glia cells, but only seldom are immigrated leucocytes found in the nerve cells.

No. 68. Oct. 12, weak in the hind legs. Oct. 14, is lying on the bottom of the cage without making any movements worth mentioning and with superficial, slow and irregular respiration. Oct. 15, dead.

Hyperaemia of the pia of the brain, the cortex in some places reddish. The vessels corresponding to the cervical and lumbar enlargements are distinctly visible, the section of the cervical cord swollen, moist, the grey matter being very red with numerous red spots and streaks, similar changes noticeable in the lumbar cord, though less pronounced; the medulla oblongata greatly congested. Microscopic examination: marked hyperaemia and intense cellular infiltration around the vessels, as well as in groups and more diffusely in the grey matter, where a large part of the immigrated cells consist of polymorphonuclear leucocytes, distinct hypertrophy of a small number of the cells in the supporting tissue. Of the nerve cells a small number have a comparatively normal aspect but most of them are degenerated, shrunken, deeply stained, homogeneous and vacuolated; a great number are invaded by numerous mono- and poly-nuclear leucocytes, others are free from these cells but more or less indented by the surrounding large, clear glia cells.

No. 69. Oct. 15, found dead to-day, yesterday nothing remarkable was observed.

The vessels on the surface of the brain injected, the cortex very red. The vessels on the surface of the spinal cord are everywhere very distinctly visible, on section the medulla oblongata vividly congested, the transverse section of the spinal cord is corresponding to both the cervical and the lumbar enlargements moist and swollen, the grey matter distinctly red and spotted with red, especially in the lumbar region. The microscopic examination shows hyperaemia, small haemorrhages, slight cellular infiltration; in

solitary places scattered groups of mostly mononuclear cells are seen, but generally neither diffuse nor perivascular cellular infiltration; distinct hypertrophy of some of the glia cells and degeneration of the majority of the nerve cells which are deeply stained, much shrunken and vacuolated, so that there often remain only small star-like or sponge-like bodies lying in the places previously occupied by the cells; enlarged glia cells have often deeply invaded the degenerated neurons.

The *intestinal* specimen, in a quantity of about 100 c. c., was inoculated into *Macacus cynomolgus* no. 53 on Oct. 1. Oct. 6, climbs slowly and runs with crooked back. Oct. 8, distinctly weak in both arms and legs, throwing the latter about when running, climbs badly, falls on jumping down, is easy to catch. Oct. 12, weak as before, especially in the hind legs. Oct. 14, is lying on the bottom of the cage perfectly paralytic in both hind legs, tries to rise with the aid of the arms but falls immediately. Oct. 15, dead.

The brain without macroscopical change. The superficial vessels corresponding to the cervical and lumbar enlargements are clearly visible, on section the spinal cord is in the lumbar enlargement rather swollen, moist and the grey matter of a reddish colour with red spots and streaks. The cervical enlargement has the same appearance, though less marked. Microscopic examination: Slight infiltration of the dura mater, also infiltration of a perivascular nature in the pia, hyperaemia of the spinal cord with solitary small haemorrhages, cellular infiltration in the grey matter, to a slight degree around the vessels, but also diffusely and in larger or smaller groups elsewhere; well marked hypertrophy of the glia cells; marked degeneration of the greater number of the nerve cells, of which a few are full of leucocytes, but the majority free from them, deeply stained, shrunken, vacuolated, with karyolysis and pyknosis of the nucleus and the body of the cell reduced through the invasion of hypertrophic glia cells.

Both the monkey infected with the specimen from the mouth and the one infected with the intestinal fluid died of poliomyelitis, the former on the 8:th day without having shown any characteristic symptoms, the latter on the 15:th day after 7 days' illness ending in complete paralysis of the hind legs. Also the con-

trol animals which were inoculated with the spinal cord from the firstnamed monkey, developed poliomyelitis, and all three died, on the sixth day.

The anatomical changes found in the spinal cords of the animals employed in these experiments are interesting. In the monkey no. 52 and its control animals nos. 67 and 68, as also in monkey no. 53 the grey matter shows both diffuse and perivascular cellular infiltration and in addition to this a more or less marked hypertrophy of the glia cells. In all the spinal cords the majority of the ganglion cells are highly degenerated and attacked by neuronophages. In one and the same section are often seen both the common leucocyte-neuronophagia and the other type, the hypertrophic glia cells eating their way into the neurons. In one place the former, in another place the latter type predominates. Thus, of the three control monkeys that were inoculated simultaneously with the same material and with the same dose, and all of which died on the same day, the first one showed chiefly glia-cell-neuronophagia, the second, no. 68, leucocyte-neuronophagia. The third control animal, no. 69, showed a slight degree of cellular infiltration of the grey matter, a marked hypertrophy of the glia cells, degeneration of the ganglion cells and glia-cell-neuronophagia, but no leucocyte-neuronophagia.

#### Case XVII.

*Sigrid Maria R—g*, a girl aged 13, from Stockholm.

Onset, on Sept. 25, with fever, faintness, headache, vomiting and constipation. Sept. 27, is weak in her legs.

She was admitted the following day to the Epidemic Hospital of Stockholm. She is stiff in her neck, cannot sit up, the muscles of the trunk paretic, can neither walk nor stand, the motor power of the legs considerably diminished, especially of the right one, the right

triceps weak, abdominal and patellar reflexes absent. Oct. 11, the power of flexion of the right elbow joint rather good, the extension very weak, cannot lift the right arm, the legs still almost completely paralyzed, she has no pain but gets easily sore and must often change position. Oct. 17, the condition somewhat improved, she can lift the right arm and the motor power of the legs has increased somewhat; the left pupil is somewhat wider than the right one, both react rather slowly. Oct. 30, the patient can only with difficulty lift the right arm, the power of flexion of the right elbow joint rather good, but the power of extension much reduced, the left arm is also paretic, though to a lesser degree than the right one, the legs are almost completely paralytic, she can only move the feet and rotate the legs a little; the plantar reflexes slightly reduced, the Achilles-tendon and patellar reflexes absent, the triceps reflexes absent on the right side, reduced on the left. Nov. 11, the general condition good, the paresis of the right arm perceptibly diminished, she is able to perform all movements though only with small strength, a slight paresis of the left arm also persisting; the patient can neither sit up in bed nor turn on the other side, but on attempting to rise the abdominal muscles contract somewhat. Both legs are still highly paralytic, only a very slight degree of flexion being possible, dorsal and plantar flexion of the feet being, on the other hand, rather good. The plantar reflexes are reduced, the Achilles-tendon and abdominal reflexes absent, and the same applies to the triceps reflexes on the right side, on the left side they are reduced. The patient is discharged to-day.

The mouth, nose, pharynx and intestine were washed on Oct. 3.

The fluid from the *mouth*, 130 c.c., was injected into *Cynocephalus hamadryas* no. 61, on Oct. 5. The Baboon was observed for several months but showed no symptoms whatever of disease.

The *intestinal* fluid was filtered both through a Heim and a Berkefeld filter, and then 130 c.c. injected into *Cynocephalus* no. 57, on Oct. 3. Oct. 4, runs less lively and climbs slowly, walks on the knuckles, especially on the right hand. Oct. 5, is easy to catch, probably somewhat weak in the left hand. Nov. 2 is still slow in its movements and climbs with exertion and jerkily. The condition remained unaltered until the last few days of December, when the animal fell ill, dying on Dec. 28. The autopsy showed recent



pneumonias in the lower lobe of the left lung and the middle lobe of the right lung.

Only the monkey inoculated with the specimen from the intestine showed any symptoms of disease. Furthermore, these symptoms were rather slight, the Baboon living for  $2\frac{1}{2}$  months subsequently to the infection and then dying of double pneumonia. However, it seems very probable that a slight infection with the virus of infantile paralysis did take place, since a certain weakness of the muscles persisted for a long time. The fact that the symptoms appeared on the day after the inoculation need not contradict this supposition, since the same occurrence has been observed in experimental animals which later on developed undoubted poliomyelitis.

#### CASE XVIII.

*Johan K—n*, a boy aged 2, from Stockholm.

The boy caught a cold in the middle of September with nasal catarrh and was since then indisposed and listless, the appetite being bad. Sept. 28, restless during the night, had pains in the neck and was tender over the cervical vertebrae. During the day the pain and tenderness in the neck ceased, but he complained of headache at the top of the head. Sept. 29, twitchings in the arms, the movements being rather uncertain, could stand on his legs but the gait was staggering.

Was admitted to the Epidemic Hospital of Stockholm on Sept. 30. He lies quiet and flaccid in his bed with the head somewhat retracted; when the head is flexed he experiences pain and when he is raised up in bed it falls backwards; he has a slight left-sided facial paresis, trembling, ataxic movements of the arms and unsteady gait; the patellar, Achilles-tendon and abdominal reflexes exaggerated. Oct. 2 the twitching of the arms and legs has considerably diminished, the pareses not increased and the patient is somewhat calmer than before, he has a slight cough and over the lungs large sibilant râles are heard. Oct. 4, the general condition improved. The patient is very much quieter, has no cough and no twitches. Oct.



10, is able to stand on his legs but cannot walk without support, the gait being even then unsteady and staggering; the left facial nerve is still rather parietic. Oct. 15, the boy has commenced to be out of bed, and is now able to walk without support. Oct. 22, the general condition very good, he walks without any difficulty and the facial paresis has diminished considerably during the last few days, being now only perceptible when the patient cries. Is discharged on Oct. 24.

The washing of the mouth and the intestine was performed on Oct. 3.

The specimen obtained from the *mouth*, 60 c.c., was injected into *Cynocephalus hamadryas* no. 59, on Oct. 4. The Baboon was observed for several months but showed no symptoms of disease.

The *intestinal* fluid, 120 c.c., was injected into *Cynocephalus* no. 58, on Oct. 3. For several months the monkey showed no symptoms of disease.

In this case we have not succeeded in demonstrating the presence of the virus of infantile paralysis either in the buccal nor in the intestinal secretion.

#### Case XIX.

*Erik Wilh. N*—g, a boy aged 3, from Stockholm.

Onset of disease on Sept. 30 with fever and profuse perspiration. On Oct. 2 he had some twitchings, mostly in the right arm and leg and on the following day he had vomitings.

Was admitted to the Epidemic Hospital of Stockholm on Oct. 5; in the morning of that same day the right arm and leg had been noticed to be weak. The general condition somewhat low but the mind clear, considerable stiffness of the neck and tenderness on pressure over the spinal column, possibly some slight paresis of the right facial nerve but nothing else from the cranial nerves, the right arm is highly parietic, with the exception of the motor power of the fingers which is intact, only a slight degree of extension of the forearm being possible; the left arm normal, the strength of the right leg somewhat reduced, of the left one normal, the patient being able to walk short distances without support, though unsteady as the right leg is apt to give way; the plantar, cremaster and abdominal reflexes normal, the triceps reflexes reduced, the patellar reflexes of

the right leg diminished, rather lively on the left side, bowels slow. Oct. 6, the general condition worse, he is more drowsy and the paresis of the right arm has increased. Oct. 8, the right leg is completely paralyzed, the left almost completely so, the right arm is still almost completely paralyzed, the patellar, cremaster and abdominal reflexes absent, no facial paresis can be observed. Oct. 9, complete paresis of both legs and also of the right arm, can only with difficulty put his left hand up to his mouth. Oct. 30, the general condition bad, the patient is fretful and moans, the head is limp, the left pupil wider than the right one, nothing from the cranial nerves, the right arm highly paretic, he can neither lift it nor bend it at the elbow joint but is able to extend it, though very feebly, the motor power of the left arm is good but that of the legs greatly diminished, especially on the right side; he can support himself on his legs, thereby holding them hyperextended, the patellar and triceps reflexes are lost. Nov. 7, the general condition rather good, a slight degree of laxity of the muscles of the neck being present, the paresis of the arms and legs about the same as on Oct. 30; is discharged.

The washing of the mouth, pharynx and intestine was done on Oct. 8.

The specimen obtained from the *mouth*, about 60 c.c. was injected, on Oct. 11, into *Macacus cynomolgus* no. 74. During a period of observation of several months no symptoms of disease were noted.

123 c.c. of the *intestinal* fluid were injected into *Macacus cynomolgus* no. 75, on Oct. 12. Oct. 23, complete paralysis of both hind legs. Oct. 25, is lying on the bottom of the cage, only moving the head. Oct. 26, same as yesterday. Oct. 27, found dead to-day.

The vessels at the surface of the brain and at the anterior aspect of the spinal cord vividly injected. The transverse section of the spinal cord is swollen and the grey matter is corresponding to the cervical and also the lumbar enlargements greyish-red discoloured. Microscopical examination: Hyperaemia and cellular infiltration of the pia, both diffuse and perivascular; the spinal cord shows hyperaemia, solitary haemorrhages, scattered accumulations of leucocytes in the vessels, marked cellular infiltration, mostly of a perivascular nature, but also diffusely and in small groups, chiefly in the grey matter but also in the white matter; great hypertrophy of some of the glia cells; the majority of the nerve cells being

intensely degenerated, only small finely granular or thread-like masses being all that is left of some of them, a small number are invaded by leucocytes although not to any greater extent.

The specimen obtained from the mouth caused no noticeable symptoms in the animal inoculated but on the other hand, the intestinal specimen, after a period of incubation of 11 days, gave rise to a typical experimental poliomyelitis with complete paralysis, death after 4 days' illness, and cellular infiltrations and leucocyte-neuronophagias in the spinal cord.

#### Case XX.

*Elsa N—g.* a girl aged 11, from Stockholm, sister to the foregoing.

Was attacked on Oct. 8 with fever and headache, rigors, pains in the arms and legs and a sensation of pain also in the back, when trying to bend the head forwards. Oct. 9, difficulty in swallowing.

On Oct. 10 she was admitted to the Epidemic Hospital of Stockholm. The general condition good, she has fever, some pain in the back and neck, when the head is bent forwards, is tender to pressure over the spinal column. No weakness of the arms, and she can get up without help or support from the hands, the movements of extension and flexion of the right leg are perhaps a little weaker than of the left one, she feels herself weaker in the right leg, is inclined to fall somewhat to the right when walking, the condition of the reflexes uncertain, she cannot be made to relax the muscles, no ataxy of the arms or legs, the movement of extending the right leg with straight knee causes some tenderness or a feeling of tightness in the calf, but not along the thigh or the sciatic nerve. Oct. 11, finds it difficult to get into the sitting posture owing to pains in the back of the head. Oct. 22, the gait normal. Nov. 3, the condition as before; the patient is discharged.

On Oct. 12 the mouth, nose and the intestine of the girl were washed.

Of the specimen obtained from the *mouth* 100 c.c. were injected into *Macacus cynomolgus* no. 78, on Oct. 16. No abnormal symp-

toms were observed but the animal was found dead on Dec. 26. Nothing remarkable had been noticed the day previously.

The superficial vessels of the brain are markedly injected, the same being the case with those of the lumbar enlargement. The spinal cord is firm, the section moist, not swollen, the grey matter being distinctly red in colour with fine red spots. Microscopic examination: Distinct hyperaemia and scattered haemorrhages but no cellular infiltration, moderate hypertrophy of some of the glia cells, intense degeneration of the majority of the nerve cells throughout the spinal cord, the cells being deeply stained, homogeneous, highly shrunken and vacuolated, only small dark, ragged masses remaining of some of them.

80 c.c. of the specimen from the *intestine* were, on Oct. 13, injected into *Macacus cynomolgus* no. 77. Oct. 14, looks ill, climbs and walks slowly, staggeringly, cannot be made to run. Oct. 15, weak in the left hind leg. Oct. 16 at noon, walks and climbs badly, is unsteady, especially on the hind legs; in the afternoon it can hardly keep upright, walks very slowly, staggeringly; when sitting the whole body trembles, is hardly able to rise from the sitting position. In the evening the animal is lying on the bottom of the cage, only moving the head a little. Oct. 17, found dead.

The vessels on the surface of the brain rather vividly injected, the surface of the spinal cord pale, some hyperaemia found only at the anterior surface of the lumbar enlargement. On section the grey matter of the spinal cord projects slightly and is distinctly greyish-red in colour. Microscopic examination of the spinal cord: Possibly a slight cellular infiltration of the pia, marked hyperaemia and numerous rather large haemorrhages in the grey matter, the perivascular lymph-spaces generally distended, no cellular infiltration; very marked hypertrophy of the greater part of the glia cells; considerable degeneration of most of the ganglion cells, some of which are, so to speak, in a state of dissolution, the rest being shrunken, homogeneous, deeply stained and vacuolated, as well as deeply excavated by the surrounding large, clear glia cells. Also some of the nerve cells of the spinal ganglia are degenerated.

The monkey inoculated with the specimen from the intestine fell ill on the day following the injection, and grew rapidly worse, dying within four days exhibiting the picture of progressive muscular



weakness, especially of the hind legs. The character of the changes found in the spinal cord prove with certainty the presence of an experimental poliomyelitis. The monkey injected with the specimen from the mouth was found dead 2 1/2 months after the inoculation without ever having previously shown any distinct symptoms of disease. The changes noticed in the spinal cord were so considerable and of such a nature, that it undoubtedly suggests poliomyelitis, especially as no other cause for death was found. On account of the long period of incubation, however, some doubt must be entertained as to the correctness of this diagnosis.

#### Case XXI.

*Johan Emil E—n*, merchant, 27 years of age, from Uppsala.

Fell ill on Oct. 6 at an hotel, having arrived in Stockholm the day before. For some time past he had been staying in Uppsala uninterruptedly with the exception of a short visit to Västerås a fortnight back and, as far as he knows, he has not come into contact with any one affected by infantile paralysis. Onset with headache, fever, rigors and profuse perspirations. On the following day vomiting also set in, he still perspired freely and had every now and then a cold shivering, in the evening he observed weakness of the legs which rapidly increased. Oct. 8, weakness of the arms too; he had twitchings in the arms and legs, especially before the onset of the paresis.

Was admitted the same day to the Epidemic Hospital of Stockholm. Mind clear, says he is tired and sleepy, but he is nevertheless unable to sleep, has only a slight headache localized to the back of the head, no aching in the back nor in the extremities. Distinct stiffness of the neck and tenderness over the upper thoracic vertebrae; nothing from the cranial nerves; the head falls backwards, when he is raised up; cannot rise himself, the abdominal muscles, however, contracting somewhat; both arms highly paretic, the motor power of the legs likewise highly reduced, he cannot bend



them but is able to extend them from the flexed position, is tender to pressure over the upper as well as over the lower extremities, especially over the nerve trunks; the patellar reflexes reduced, the plantar, Achilles-tendon, cremaster, abdominal and triceps reflexes absent, is unable to pass his water, bowels constipated. Oct. 9, during the day a considerable change for the worse with regard to his condition, the laxity of the muscles increased, the patient lying almost motionless, difficulty in swallowing has also set in, and the respiration is very much hampered, strained and superficial, slight cyanosis; died in the afternoon.

On Oct. 9 the washing of the mouth and intestine of the patient was done.

The specimen obtained from the *mouth*, 100 c.c., was injected into *Macacus cynomolgus* no. 70, on Oct. 10. Oct. 27, is lying on the bottom of the cage completely paralytic, breathing slowly and superficially. Oct. 28, dead.

The blood vessels on the surface of the brain greatly distended, the cortex distinctly red. The vessels at the anterior surface of the spinal cord plainly visible, on section the spinal cord everywhere moist but not swollen, the grey matter markedly reddish. Microscopic examination: Vivid hyperaemia and rather large haemorrhages in the grey matter, traces of a slight cellular infiltration in different places; distinct hypertrophy of the majority of the glia cells; pronounced degeneration of most of the nerve cells which are either very pale and finely granular or else shrunken, deeply stained, homogeneous, highly vacuolated and attacked by the surrounding, enlarged glia cells which sometimes have digged their way deeply into the nerve cells.

100 c.c. of the specimen from the *intestine* were injected into *Macacus cynomolgus* no. 71, on Oct. 10, and 105 c.c. into *Macacus cynomolgus* no. 76, on Oct. 12.

No. 71. Nov. 2, complete paralysis of the left arm and hand; the animal is weak in the legs and can neither walk nor climb, is able to sit upright and to rise, although with some difficulty, trembles and staggers; when trying to move it falls down and it can only drag itself somewhat along by the aid of the right arm and the hind-legs. In the afternoon the animal is lying on the bottom of the cage, almost completely paralytic. Nov. 4, dead.

The vessels on the surface of the brain are vividly injected,

a marked injection being found also on the anterior surface of the spinal cord. On section the cord is smooth, not swollen, showing very sharp distinction between the white and the grey matter which in the medulla oblongata is plainly of a greyish-red colour with red dots and streaks. Microscopic examination: Rather a marked cellular infiltration of the pia and in the anterior fissure, considerable hyperaemia of the spinal cord and large haemorrhages in the grey matter, perivascular and diffuse infiltration of chiefly mononuclear cells; no distinct hypertrophy of the glia cells; marked degeneration of the nerve cells which often are greatly encroached upon by, as a rule, mononuclear leucocytes.

*Cercopithecus Burnettii* no. 139 was, on Nov. 8, injected intraperitoneally and into both sciatic nerves with a non-filtered emulsion of the spinal cord from the foregoing monkey. Nov. 29, is lying on the bottom of the cage, moving but very little, a rather marked ptosis of both eye-lids and deviation of the right bulb outwards. In the evening in a dying condition; killed.

The surface of the brain is pale and the same applies to that of the spinal cord. On section the spinal cord does not swell, the grey matter is distinctly marked, its colour in the lumbar enlargement distinctly, though not highly, reddish. The left lung moderately indurated (probably after a pneumonia). Microscopic examination: No obvious changes to be found either in the medulla oblongata nor in the spinal cord.

No. 76. Oct. 16, climbs rather unsteadily. In the evening, climbs slowly, cannot be made to run, walks with a limp, paretic in the left arm, is easily pushed over. Oct. 17, dying, respiration abdominal, slow and irregular. Oct. 18, found dead.

The brain without macroscopic changes. The vessels corresponding to the lumbar and the lower portion of the dorsal cords are plainly visible, on section the spinal cord is, in the lumbar region, moist, but not swollen, the grey matter indistinct and of a somewhat reddish colour around the commissure. Microscopic examination: Hyperaemia of the grey matter but no haemorrhages, in some places slight signs of cellular infiltration; the glia cells unchanged; the nerve cells generally somewhat shrunken and deeply stained, though showing in places a distinct tigroid substance, others again being homogeneous and more or less vacuolated.

With an emulsion of the spinal cord two other monkeys were inoculated. *Cynocephalus hamadryas* no. 90 was, on Oct. 20, in-

jected into both sciatic nerves with non-filtered emulsion. No symptoms of disease were observed afterwards.

Some non-filtered emulsion was, on Nov. 9, injected into the sciatic nerve, and 60 c.c. filtered emulsion into the peritoneal cavity of *Cercopithecus Burnetti* no. 141. Nov. 21, falls on its face when jumping, weak in the right fore leg. Nov. 25, has during the last few days mostly been crouching in the cage but has been able to run fairly well. To-day the animal cannot be made to run, only walk, the weakness seems to be more pronounced in the hind legs, but no isolated, distinct paresis can be discovered. In the evening the animal walks only slowly with bent knees, possibly paretic in the muscles of the hip-joints. Nov. 26, dead.

Rather numerous haemorrhages of the size of a pin's head in the pia corresponding to the convexity of the brain, the membranes otherwise being rather pale, at the apex of each frontal lobe accumulations of small haemorrhages are seen over areas about the size of a pea. The surface of the spinal cord is pale, the section swollen, the grey matter being indistinctly marked, not reddish discoloured. Microscopic examination: No pronounced hyperaemia and no cellular infiltration, accumulation of white corpuscles in the vessels and slight perivascular infiltration in the medulla oblongata; distinct hypertrophy of a large part of the glia cells, considerable degeneration of the majority of the ganglion cells, which are shrunken, homogeneous and markedly vacuolated, the surrounding glia cells having eaten their way deeply into some of them.

The animal inoculated with the specimen from the mouth was attacked after 17 days, became completely paralytic, and died on the following day. The spinal cord showed an advanced destruction of the nerve cells but scarcely any changes of an infiltrative nature. Of the animals infected with the intestinal specimen the first, no. 71, became completely paralytic in one arm after 23 days, died two days later and showed typical infiltrative changes in the spinal cord. Its control animal, on the other hand, showed a picture which was very little typical of the disease in question and very slight changes were found in the spinal cord.

The second monkey, no. 76, was attacked after 4 days, developed a marked paresis of one arm and died after an illness of less than two days. The spinal cord showed scarcely any cellular infiltration and only a comparatively slight degeneration of the nerve cells. Injected emulsion of the spinal cord caused a high degree of general muscular weakness and death of one of the control-animals. Some slight perivascular infiltration was found in the medulla oblongata of this animal, as also a very marked degeneration of the nerve cells of the entire spinal cord.

#### Case XXII.

*Arvid Ernfrid S*—g, a messenger boy aged 17, from Stockholm.

Onset on Oct. 5 with pains in the back, especially in the lumbar region and in the neck. Still he kept on working until in the evening of Oct. 7, when he was obliged to go to bed, had fever, headache, vomiting and perspired at intervals; felt drowsy and sleepy but could not go to sleep. In the morning of Oct. 9, he observed that he could not stand on his legs, he had no urinary trouble and the bowels acted normally.

Was admitted to the Epidemic Hospital of Stockholm the same day.

Mind clear, feels tired and sleepy, has slight aching pain in the neck and in the small of the back but experiences no tenderness on palpation of the spinal column, the cervical muscles flaccid, the head falling backwards when an attempt is made to make him sit up in bed, which he cannot do by himself, the abdominal muscles not even contracting; nothing from the cranial nerves; marked paresis of both arms, the movements of the shoulder-joints can only be performed incompletely, all the movements of the elbow- and wrist-joints can be performed but only with reduced strength, the legs are also highly paretic, the movements of flexion cannot be performed at all and the movements of extension are done very feebly, the movements of the feet and toes considerably reduced, plantar, Achilles-tendon, cremaster, abdominal and



triceps reflexes absent. Oct. 10, the patient has during the night slept at intervals, at 8 o'clock in the morning he began to experience difficulty in breathing, the respiration grew superficial, strained, breathing with the nasal wings and rather marked cyanosis setting in, profuse perspiration, no difficulty in swallowing, mind clear. During the day the condition became gradually aggravated, the respiratory difficulty increased, during the last few hours there were at times rather long respiratory pauses, mind clear until an hour or two before death, which occurred in the evening.

On<sup>n</sup> Nov. 9 the buccal cavity and the intestine were washed.

Of the specimen from the *mouth* 100 c.c. were, on Oct. 11, injected into *Macacus cynomolgus* no. 72. Oct. 18, complete paralysis of the left leg, but the animal still climbs fairly well. Later in the same day complete paralysis of both legs, drags itself along on the front legs. Oct. 20, dead.

The vessels on the surface of the brain rather vividly injected, the distinction between cortex and medullary substance pretty well marked. The surface of the spinal cord pale, the section does not swell and the grey matter is not very distinct, being most marked in the lumbar enlargement where also a number of fine, red spots are visible. Microscopic examination: Slight cellular infiltration of the pia, more marked in the anterior fissure and around most of the vessels of the white and especially the grey matter of the lumbar cord which, besides hyperaemia and haemorrhages, also shows considerable infiltration, diffuse and in groups, of chiefly mononuclear leucocytes; distinct hypertrophy of a small number of the glia cells, nearly all the ganglion-cells being highly degenerated and containing a large number of immigrated, chiefly mononuclear leucocytes (Fig. 1). In the cervical cord leucocyte-neuronophagias are as a rule absent, the nerve-cells being shrunken, deeply stained, homogeneous, vacuolated and notched by the surrounding large, clear glia-cells.

100 c.c. of the specimen from the *intestine* were on Oct. 11 injected into *Macacus cynomolgus* no. 73. Oct. 14, climbs slowly, runs joggingly, moves the left hind-leg abnormally. Oct. 15, paretic in the left hind-leg. Oct. 16, climbs and runs very badly and staggeringly. During observation to-day the monkey was seized by an attack of convulsions lasting a few minutes, it then was lying



as if lifeless for a while, but came round again and was able to get up. In the evening the animal is sitting swaying the body, keeping the back curved and the head bent deeply downwards, if pushed over, it can only manage to get up with the greatest difficulty; dying in the evening. Oct. 17, dead.

The cortex of the brain in some places distinctly reddish. The vessels on the surface of the spinal cord plainly visible all along fissura anterior and at the posterior aspect of the lumbar cord, on section the spinal cord is moist but not swollen, very marked reddish discoloration of the grey matter in the dorsal region, less pronounced in the cervical and lumbar cords. Microscopic examination: Moderate degree of hyperaemia, scattered haemorrhages, but scarcely any distinct cellular infiltration; the glia cells considerably enlarged, clear, transparent; degeneration of the nerve cells with far advanced glia-cell-neuronophagia.

On Oct. 20 *Cynocephalus hamadryas* no. 93 was inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord and on Nov. 8 *Cercopithecus Burnetti* no. 140 both intraperitoneally and into one sciatic nerve with filtered emulsion.

No. 93. Nov. 10, the Baboon has a rather pronounced tremor, is ataxic in its movements and climbs only with difficulty, sometimes falling on its nose when trying to run, if caught from the back and held up, it kicks with all four extremities just like a jumping-jack, does not seem to suffer from any muscular weakness. When disturbed after having been sitting still for some time, the animal is often seized by convulsions, rushing now here and now there without any motive, at such times often falling on the nose. Nov. 11, looks somewhat less well than yesterday, no convulsions have been observed, but the animal finds it difficult to co-ordinate its movements, reeling hither and thither, oscillating with the head; is weak in the hind legs, limps in the left, climbs only with difficulty, has become strikingly bad-tempered, fights with the arms and wants to bite, is able to hold an apple with its hands and to eat it. In the afternoon the Baboon cannot rise on the hind legs, moves by dragging itself along on the seat, the right hand in the position of radial paresis, if pushed over, it has great difficulty in rising. Oct. 12, is lying on the bottom of the cage completely paralyzed in the hind legs, moves the head, arms and tail a little, left-sided ptosis. Nov. 11, is lying almost motionless, only turning the head and body somewhat. Nov. 14, found dead.

Marked hyperaemia of the superficial vessels of the brain, the cerebral cortex is greyish-red and the substance of the brain in general more than usually spotted with blood. The vessels of the spinal cord distinctly visible. On section the spinal cord moderately swollen and moist, the grey matter greyishly-red discoloured with numerous red spots and streaks. Microscopic examination: Hyperaemia and cellular infiltration of the pia mater, marked hyperaemia of the spinal cord, rather numerous and sometimes large haemorrhages, cellular infiltration around the vessels, the grey matter also showing a considerable infiltration, both diffuse and in groups, the cells mostly being mononuclear; marked hypertrophy of the majority of the glia cells; extensive degeneration of the nerve cells which are either inundated by leucocytes, or else deeply hollowed out by enlarged glia cells, solitary ones being encroached upon by both kinds of cells; the changes are most pronounced in the lumbar region.

No. 140. Nov. 16, more slow in its movements than before. Nov. 20, runs somewhat joltingly but otherwise rather well, possibly weak in the fore legs. Nov. 25, has during the last days been sitting huddled up in one spot; is to-day lying on the bottom of the cage and moves but very little; found dead in the evening.

The vessels on the surface of the brain, especially at the base vividly injected, a marked contrast noticeable between cortex and medullary substance. The surface of the spinal cord pale, the section moist but not swollen, the grey matter everywhere slightly greyish-red. Microscopic examination: Marked hyperaemia and solitary haemorrhages, but no cellular infiltration; some of the glia cells distinctly enlarged; the ganglion cells generally dark and rather homogeneous, some of them being, besides, shrunken and vacuolated, enlarged glia cells often having eaten their way into them, the changes however, on the whole not very pronounced.

The monkey which had been inoculated with the specimen from the mouth developed a typical poliomyelitis with complete paralysis of both legs, on the seventh day. It died on the ninth day and the spinal cord showed typical changes, cellular infiltration and leucocyte-neuronophagia in the grey matter. The monkey which was injected with the intestinal spe-

cimen died on the fifth day after only 24 hours' illness, this case being, however, not so characteristic as that of the preceding monkey. No isolated, flaccid paralysis was observed but only paresis, followed by general muscular weakness and finally by a general paralysis. The spinal cord showed degeneration of the nerve cells and glia-cell-neuronophagia. Two control animals were inoculated with emulsion of the spinal cord. One of them developed a paralysis of a descending type, commencing with ataxia and general convulsions. The spinal cord showed marked cellular infiltration of the grey matter and numerous leucocyte-neuronophagias. In the second control animal the disease developed in about the same way as in the original monkey, and the pathological changes of the spinal cord were of very much the same character too. Thus the disease from which the monkey suffered, and which was caused by inoculation of the intestinal fluid, was also poliomyelitis, and the investigation has proved, that the specimen from both the mouth and the intestine contained the microbe of infantile paralysis.

#### Case XXIII.

*Harry R—m*, 4 years old, from Stockholm.

Onset on Oct. 9 with stiffness of the neck, headache and fever. In the evening it was observed that his gait was rather unsteady and reeling. Oct. 10, the headache gone, but the patient felt tired and sleepy, had cold shiverings. Oct. 11, in the morning he had an attack of twitching all over the body lasting about 15 minutes; cross-tempered, no perspiration.

The boy was admitted the same day to the Epidemic Hospital of Stockholm. He is somewhat drowsy and obstinate, marked stiffness of the neck but evidently no pain on palpation over the spinal column, nothing from the cranial nerves, the power of the muscles of the arms, trunk and legs apparently not reduced; the

left leg perhaps being a little weaker than the right one, the gait rather reeling; he is able to walk without support, but he deviates to the left; the plantar, patellar and triceps reflexes somewhat increased, the abdominal and cremaster reflexes normal. Oct. 14, the stiffness of the neck gone, the patient walks with a limp in the left leg; the patellar reflexes increased. Nov. 11, the general condition good, the gait normal the patellar reflexes lively; is discharged.

On Oct 12 the mouth and intestine were washed.

Of the specimen obtained from the *mouth*, 100 c.c. were injected into *Macacus cynomolgus* no. 82, on Oct. 17. The monkey was found dead on Oct. 22; nothing unusual had been previously observed.

The vessels on the surface of the brain fairly distended, sharp distinction between cortex and medullary substance. The superficial vessels of the spinal cord slightly injected both at the anterior and posterior aspects, on section the spinal cord everywhere much swollen and moist, the grey matter distinctly of a reddish hue. Microscopic examination: Intense hyperaemia and numerous small haemorrhages, but no cellular infiltration, the majority of the glia cells being enlarged, clear and transparent; rather pronounced degeneration of the nerve cells, the nucleus shrunken, diffusely and deeply stained, the cell body in many places shrunken, deeply stained, homogeneous and vacuolated and often deeply hollowed out by the surrounding, enlarged, clear glia cells, a small number of the nerve cells, again, having a light, homogeneous or exceedingly finely granular protoplasm, looking as if in a state of dissolution.

*Macacus rhesus* no. 100 was inoculated with a non-filtered emulsion of the spinal cord into both sciatic nerves, on Oct. 24. Oct. 27, does not climb with the same agility as before. Nov. 3, climbs with exertion and with jerks, looks thin. The condition unaltered until Dec. 5. Climbs remarkably slowly, can hardly be made to run but walks with slow and solemn steps, poor and thin, bowels loose. Dec. 6, is lying almost motionless on the bottom of the cage. Dec. 7, dead.

The pia of the brain greatly injected, likewise the pia of the spinal cord, at the posterior aspect of the swellings. The section of the spinal cord swells somewhat, the grey matter is everywhere distinctly reddishly discoloured. Microscopic exami-



nation: Intense hyperaemia and small haemorrhages in different places but no cellular infiltration; marked hypertrophy of the majority of the glia cells, considerable degeneration of the ganglion cells into which the surrounding, enlarged glia cells have penetrated very far. The changes are most pronounced in the dorsal region.

Of the fluid obtained by washing the *intestine*, 140 c.c. were injected into *Macacus cynomolgus* no. 79, on Oct. 16. The animal was found dead the following day. The abdominal cavity contained 30 c.c. clear fluid, in which were found solitary bacteria, the peritoneum was smooth and shiny, and no changes were observed in any other organs.

The monkey which had been inoculated with the specimen from the mouth died suddenly on the fourth day after the inoculation. The spinal cord showed marked changes, especially a wide-spread degeneration of the nerve cells, but no infiltration. The control animal, which had been infected with the spinal cord, was attacked after three days, but did not die until after about 6 weeks' illness with symptoms of progressive marasmus and muscular weakness. The spinal cord showed almost the same changes as those found in the preceding monkey. As nothing else could be found to explain the fatal termination, it seems only right to make the diagnosis of experimental poliomyelitis.

#### Case XXIV.

*Astrid L—n*, 3 years of age, from Stockholm.

Onset during the night of Oct. 12 with fever and headache, as well as tenderness in the arms and legs. On Oct. 13 the mother noticed that the gait of the girl was unsteady and reeling. On Oct. 14 she was paretic in the left arm.

Was admitted, on Oct. 15, to the Epidemic Hospital of Stockholm. The general condition good, nothing in the pharynx, she experiences distinct pain when trying to bend the head towards the chest, the left arm is tender to pressure, the facial nerves not involved, the movements of the eyes are co-ordinated and the pupils react, the left arm paretic, she can rise into a sitting pos-



tureal though with difficulty and much groaning; the movements of the legs normal, the gait being, however, rather uncertain and staggering; the patellar reflexes increased, the triceps reflexes possibly exaggerated on the right, absent on the left side. Oct. 27, can with difficulty lift the left arm, the gait still somewhat uncertain and staggering, the patellar reflexes increased, the triceps reflexes lively on the right side, reduced on the left. Oct. 29, walks rather well. Nov. 11, the general condition good, the power of the left arm considerably increased, the gait normal; is discharged.

On Oct. 15 washing of the mouth and intestine was performed on the girl.

Of the specimen from the *mouth* 120 c.c. were injected into *Macacus cynomolgus* no. 86, on Oct. 19. The animal was observed for more than three months but showed no abnormal symptoms.

Of the specimen obtained from the *intestine* 60 c.c. were injected, on Oct. 18, into *Macacus cynomolgus* no. 85. Oct. 19, runs and climbs rather slowly, when jumping it falls down on its nose. Oct. 22, climbs slowly, does not like to run, possibly weak in the left hind leg. Oct. 23, paresis of the left arm, falls on its nose. Oct. 25, the left hand in the position of radial paresis, gait staggering. Oct. 26, lying on the bottom of the cage, moving only very slightly, right-sided ptosis. Oct. 27, dead.

The superficial vessels of the brain and spinal cord moderately injected. On section, the spinal cord is swollen and the grey matter of a distinct greyish-red colour, especially in the dorsal and lumbar regions. Microscopic examination: Hyperaemia, but no haemorrhages, the grey matter being in some places, especially in the vicinity of some vessels, rather rich in cells, distinct hypertrophy of some of the glia cells, very pronounced degeneration of the majority of the nerve cells which are shrunken, deeply stained, homogeneous and much reduced by glia-cell-neuronophagia, mostly only small, irregular masses being left.

In the case of this patient we only succeeded in demonstrating the presence of the microorganism of infantile paralysis in the intestinal specimen, which gave rise to characteristic pareses in the animal used for inoculation. In the spinal cord a considerable destruction of the nerve cells was found.

## Cases XXV.

*Erik S—m*, 5 years old, from Stockholm.

Was attacked during the night of Oct. 13 with pain in the legs, back and neck and had fever. On the following day the pain in the legs and back passed off, and there remained only a slight stiffness of the neck; neither in the arms nor in the legs could any weakness be observed.

Was admitted to the Epidemic Hospital of Stockholm on Oct. 14. Mind clear, does not complain of any pain, a slight stiffness of the neck is present but no pain is felt when the head is bent forwards, and there is no tenderness to pressure over the spine, no involvement of the cranial nerves; has unrestricted motile power and normal strength in his arms and legs, but when he stretches his hands towards some given object, a certain degree of trembling is observed in them, walks on the toes; the patellar, Achilles-tendon, abdominal and triceps reflexes increased, facial phenomenon on both sides. Oct. 17, is still somewhat stiff in the neck and has somewhat increased reflexes but no pareses. Nov. 12, the patellar reflexes are still somewhat livelier than normally, but otherwise no objective signs; is discharged.

The boy's mouth, nose and intestine were washed on Oct. 15.

On Oct. 18 two *Macaci cynomolgi* nos. 83 and 84 were injected with the specimen from the *mouth*, each animal receiving 100 c.c.

No. 83. Oct. 19, runs slowly, but any apparent weakness of the legs is not to be observed. Oct. 22, does not climb as quickly as previously. Oct. 28, is lying on the bottom of the cage completely paralyzed in all the extremities, breathes slowly and irregularly. Oct. 29, dead.

The pia of the brain rather vividly injected, but no perceptible hyperaemia of the membranes of the spinal cord. On section, the spinal cord does not swell, the grey matter is sharply marked and in the cervical enlargement distinctly greyish-red. Microscopic examination: Marked hyperaemia and rather numerous haemorrhages in the grey matter, but no evident cellular infiltration; hypertrophy of a large number of the glia cells, especially around the cells of the anterior horns; the main part of the nerve cells degenerated, shrunken, torn at the edges, homogeneous, deeply

stained, considerably vacuolated and encroached upon by the surrounding large, clear glia cells.

Two monkeys, *Macaci rhesi* nos. 117 and 118, were inoculated with a non-filtered emulsion of the spinal cord. Neither of them showed any signs of disease.

No. 84. Oct. 19, runs slowly, when jumping evidently weak in the extremities. Oct. 22, paretic in both arms, but more so in the right one, the right hand being held in the position of radial paresis, walks slowly and sometimes falls on its nose. Oct. 23, weak also in the left hind leg. Oct. 25, cannot use the fore legs, when walking jumping about on the hind legs. Oct. 27, is sitting motionless holding the hands in the position of radial paresis. Oct. 28, dead.

A moderate degree of hyperaemia of the pia of the brain, that of the spinal cord being pale. On section, the spinal cord swollen, the grey matter distinctly marked but not reddish. Microscopic examination: Marked hyperaemia and scattered haemorrhages, scarcely any quite distinct cellular infiltration but in some places an increase in the number of cells surrounding the nerve cells; the greater number of the glia cells greatly enlarged, clear, transparent; the nerve cells generally degenerated, the nucleus shrunken, deeply and diffusely stained, the cell body likewise shrunken and saturated with dye, homogeneous, vacuolated and deeply hollowed out by surrounding large, clear cells.

Two monkeys were, on Oct. 17, inoculated with the fluid obtained from the *intestine*. *Macacus cynomolgus* no. 80 received 80 c.c., and no. 81, 38 c.c.

No. 80. Oct. 18, looks ill, cannot keep upright, crawls slowly along all the while shaking all over the body. Oct. 19, runs slowly and unsteadily, falls easily on its hind legs and rolls readily over when pushed a little. Oct. 20, dead.

The brain without macroscopical change. The vessels corresponding to the lumbar and dorsal portions of the spinal cord moderately injected, the section of the spinal cord showing no distinct changes, the grey matter possibly of a slight reddish tint. Microscopic examination: Slight hyperaemia, no haemorrhages and no distinct cellular infiltration; some glia cells, especially those around the cells of the anterior horns, are large, clear and transparent; the nerve cells present in part a normal appearance with distinct tigroid substance, others again are degenerated, homogeneous and vacuolated,

and either pale, as if in a state of dissolution, or shrunken and saturated with dye.

*Macacus rhesus* no. 104 was inoculated into both sciatic nerves with a non-filtered emulsion of the spinal cord, on Oct. 26. Nov. 18, is sitting still on the bottom of the cage, possibly somewhat weak in the feet, dyspnoea. In the afternoon very poor, severe dyspnoea. Nov. 18, died in the evening.

The soft membranes of the brain, as well as those of the spinal cord hyperaemic, a sharp contrast noticeable between the cerebral cortex and medullary substance. The section of the spinal cord markedly swollen in all parts of the cord, and the grey matter everywhere distinctly marked and of a rather deep greyish-red colour. Double-sided recent pleurisy and right-sided recent pneumonia. Microscopic examination: The brain shows in the vicinity of the central convolutions an intense hyperaemia of the pia, the injection of the cortex being somewhat less pronounced, some vessels contain numerous leucocytes, some of them being also surrounded by more cells than normally, solitary, small haemorrhages and hyaline thrombs likewise being found. The spinal cord shows marked hyperaemia and oedema of the grey matter, no quite distinct cellular infiltration, but obvious hypertrophy of some of the glia cells; the greater part of the nerve cells more or less changed, the nucleus slightly and diffusely or not at all stained, the cell body, on the contrary, saturated with dye, sometimes showing all the same slight signs of a tigroid substance, shrunken and vacuolated.

No. 81. Dec. 9, climbs badly. In the afternoon the condition aggravated, runs slowly with a limp, when trying to jump it falls on its nose. Dec. 10, dead.

The brain macroscopically without any change. The superficial vessels of the spinal cord not particularly distended, the section of the spinal cord is moist and swollen, the grey matter has everywhere a distinct reddish tint. Microscopic examination: Rather marked hyperaemia and solitary haemorrhages in the grey matter, no distinct cellular infiltration but well marked hypertrophy of the majority of the glia cells; the ganglion cells being greatly and to a large extent degenerated, shrunken, deeply stained and highly vacuolated, besides which the surrounding hypertrophic glia cells have eaten themselves deeply into them, small dark and torn masses often being all that is left of the cells of the anterior horns.



Both monkeys inoculated with the specimen from the mouth were attacked on the day after the injection, and both died at about the same time, i. e. on the 10:h—11:th day. One of them showed no isolated paralysis, but the other one, on the contrary, developed a marked paresis of both arms which could not be used in walking. The spinal cords of both these animals presented marked changes, chiefly in the nerve cells, but no distinct cellular infiltration nor any leucocyte-neuronophagia. The two control monkeys inoculated with the spinal cord from one of the original monkeys remained well.

Of the two monkeys injected with the intestinal specimen, the one was attacked on the day after the injection, developed tremor and general muscular weakness and died on the third day. The changes in the spinal cord were not very marked. A control animal to this one died on the 23:rd day of recent pneumonia and pleurisy. This animal showed, however, such considerable changes in the central nervous system that they could hardly have been caused by the secondary infection alone. The other monkey infected with the intestinal fluid was not attacked until after about 7 weeks and died suddenly. The nerve cells of the spinal cord were highly degenerated, but neither cellular infiltration nor any leucocyte-neuronophagia were found. Through the experiments it must undoubtedly be regarded as proved, that the microbe of infantile paralysis was present on both the membranes examined.

#### Case XXVI.

*Gösta E—t*, 3 yars old, from Stockholm.

Onset on Oct. 14, was drowsy and felt unwell, vomited and had twitchings in the left upper and lower extremities.

On Oct. 16 he was admitted to the Epidemic Hospital of Stockholm. The patient is somnolent, does not react when spoken to, turns and twists and offers great resistance during the examination, no stiffness of the neck, but possibly some tenderness on pressure over the spine, the patient during this manipulation bending himself far backwards; the condition of the cranial nerves cannot be closely examined, owing to the unclear state of mind of the patient, the two halves of the face equal, the muscles of the neck flaccid, the power of the arms and legs evidently not reduced, he offers great resistance to movements, all the reflexes are lively, the patellar reflexes possibly increased; the pharynx slightly reddened; has vomited several times during the day. Oct. 17, he is rather restless; is lying in opisthotonos position, tosses to and from in bed; has to be fed by means of a tube. Oct. 23, marked strabismus, slight paresis of the external rectus muscle on both sides. Oct. 25, no flaccidity of the muscles of the neck. Nov. 12, the general condition good; no pareses can be observed and the reflexes are normal. Discharged.

The mouth and intestine of the boy were washed on Oct. 16.

Of the specimen from the *mouth*, 100 c.c. were injected into *Macacus cynomolgus* no. 88, on Oct. 19. This monkey never developed any symptoms of disease.

Of the specimen from the *intestine*, 100 c.c. were, on Oct. 19, injected into *Cynocephalus hamadryas* no. 89. Oct. 21, is lying almost motionless on the bottom of the cage; is very cyanotic. Died in the evening.

Marked hyperaemia of the superficial vessels of the brain, the cortex has a very pronounced reddish colour and the section is moist. The spinal cord not obviously hyperaemic, on section not swollen but moist, the grey matter having a very distinct greyish-red colour. Microscopic examination: Marked hyperaemia and numerous large haemorrhages in the grey matter but hardly any distinct cellular infiltration, considerable hypertrophy of a great deal of the glia cells, some ganglion cells being of a comparatively normal appearance, others again shrunken, deeply stained, homogeneous and vacuolated.

*Macacus rhesus* no. 99 was, on Oct. 24, infected into both sciatic nerves with a non-filtered emulsion of the spinal cord of the pre-

ceding monkey. Oct. 27, almost complete paresis of both hind legs. Oct. 28, died to-day.

The vessels on the surface of the spinal cord and brain, more especially over pons and medulla oblongata, are most vividly injected, the section of the spinal cord is swollen and the grey matter is distinctly marked, but scarcely reddish in colour. Beneath the right sciatic nerve is an abscess of about the size of a pea, with a few bacteria, but the nerve itself is free. Microscopic examination: Moderate hyperaemia and oedema in the grey matter but no distinct cellular infiltration; great hypertrophy of most of the glia cells; degeneration of the greater part of the nerve cells which are either very pale, finely granular or else dark, homogeneous, highly vacuolated and deeply infiltrated by the enlarged glia cells, small, dark, irregular masses often being all that is left.

It was only the specimen from the intestine that gave rise to any symptoms of disease in the inoculated animal, this being attacked and dying suddenly on the second day after the inoculation. The changes found in the ganglion cells of the spinal cord were comparatively less pronounced. Its control animal, on the other hand, developed a complete paralysis of the hind legs and showed an extensive destruction of the ganglion cells of the spinal cord, whereas cellular infiltration and leucocyte-neuronophagia were not found.

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Amongst the patients who have been the subjects of this investigation both *typical and atypical, slight and severe cases* are to be found. Three of the latter were fatal. Most of them have exhibited considerable pareses while the remainder have presented only very slight effects. Other symptoms from the nervous system have, however, made the diagnosis certain in all cases. Subsequent experiments on animals has confirmed the diagnoses. The results are summarised in the following table.

Table II.

	<i>Mouth</i>	<i>Intestine</i>
Gunhild G—n	+	—
Ingrid S—g	$\begin{array}{c} \diagup + \\ + - + \\ \diagdown + \end{array}$	+
Sigrid Maria R—g	o	+
Johan K—n	o	o
Erik Wilhelm N—g	o	+
Elsa N—g	+	+
Johan Emil E—n	+	$\begin{array}{c} + - + ? \\ + - o \\ \diagdown + \end{array}$
Arvid Ernfrid S—g	+	$\begin{array}{c} + < + \\ + < + \end{array}$
Harry R—m	+	—
Astrid L—n	o	+
Erik S—m	$\begin{array}{c} + < o \\ + < o \end{array}$	$\begin{array}{c} + - + ? \\ + \end{array}$
Gösta E—t	$\begin{array}{c} + \\ o \end{array}$	$\begin{array}{c} + \\ + - + \end{array}$
	<hr/> 7 +	<hr/> 9 +
	5 o	1 o
	<hr/> 12	<hr/> 10

Only in the cases of one living subject and one dead body we have entirely failed to demonstrate the presence of the micro-organism of infantile paralysis on the mucous membranes. In the case of another patient, the monkey that was inoculated showed only slight symptoms. It is, however, to be remarked, that when investigating these two patients we only had rather strong Baboons at our disposal, being probably less susceptible to an infection with this virus than the Macaci, which were mostly used in our experiments. At all events a much smaller percentage of the former than of the latter were attacked. If the issue of the above investiga-



tions on both living and dead bodies be summarised, the final result will show *that the presence of the microbe has been detected on one of the examined membranes in 24 cases out of 26*. We consider it fully justifiable to place the results of both series of investigations side by side. In most cases, the material used for the experiments was taken from the dead bodies so soon after death, that there is no reason for supposing that the microbe could have passed out to the surface of the mucous membranes from the interior of the body.

In order to estimate the practical value of our investigations, it must be taken into consideration that the inoculation of monkeys cannot be said to be a very reliable method to demonstrate the presence or absence of the micro-organism of infantile paralysis.. Also attempts to infect with the spinal cord, which during the acute stage no doubt always contains large quantities of the virus, have often failed, both when the material has come from cases of infantile paralysis in human beings and from cases of experimental poliomyelitis in monkeys.

Considering these difficulties in demonstrating the presence of the microbe, we consider ourselves fully justified in drawing the conclusion from the results obtained, *that the virus in all probability is always present on the mucous membranes of the nose, mouth, pharynx and intestine of persons affected by infantile paralysis, during the acute stage of the disease. It is obvious that the knowledge of this fact is of the greatest importance in formulating our views regarding the mode of transmission of the disease.*

Since the time when FLEXNER and LEWIS succeeded in demonstrating the virus on the nasal mucous membrane of the monkey after intracerebral inocula-

tion, attention has been drawn to the fact that the microbe could, perhaps, in this way leave the infected organism and spread further. LANDSTEINER, LEVADITI and DANULESCO have also demonstrated in monkeys that the virus can really pass through the mucous membrane and from the interior of the body get out into the secretion. It is obvious, however, that another possibility might be conceived, viz. that the microbe has been carried to the mucous membrane from outside, has multiplied in the secretion and finally perhaps penetrated the mucous membrane and caused the infection. We shall later on revert to this question and at the same time give reasons in support of this probability.

Noteworthy is the great difference in the positive results obtained in the investigation of the buccal respectively intestinal fluids, in the living subject: 7 positive out of 12 in the former case, and 9 positive out of 10 in the latter case. Since the number of cases examined is not very great and the difference obtained in the two kinds of specimens from dead bodies is less marked, probably no definite conclusion can be drawn from the fact mentioned.

\*            \*            \*

c) Investigations regarding the presence of the micro-organism of infantile paralysis on the mucous membranes of abortive cases and healthy persons.

Through previous investigations of LEINER and v. WIESNER, it is known that the virus of infantile paralysis is present in the blood, at least during some period

of the disease, even though it may not exist in very great quantity. From our investigations, an account of which has just been given, it may be concluded further that the microbe is present, in all probability constantly, in the secretions from the mouth, nose, pharynx and trachea, as well as in the intestinal secretion of persons attacked by infantile paralysis. It is thus obvious that the blood of persons affected by infantile paralysis, as well as the secretions from their mucous membranes, may be considered to be infective and able to play some rôle in the transmission of the disease. Investigations undertaken with the view of attempting to unravel the manner of transmission of the contagion must therefore consider both these sources of infection and investigate the possibility of a propagation of the virus from them i. e.

*1:o the probability of a transport of infected secretions from one affected person to another, either directly or by the intermediary of some other living being, man or animal, or lastly with dead objects as intermediary agents;*

*2:o the probability of a transmission of the virus by means of blood-sucking insects.*

It must at once be admitted that the demonstration of the virus on the mucous membranes of persons attacked by infantile paralysis is insufficient to explain the manner of transmission of the disease. It very often occurs, that those infected have never had any intercourse with patients presenting distinct pareses. In order to be able to associate with any degree of probability the origin of the disease with a direct spreading of the microbe, it is evidently necessary to prove the presence of the virus not only in patients with marked pareses, but also in other individuals. Perhaps there are types

of the disease caused by the same virus but showing no pareses, whilst possibly the microbe may be present even in perfectly healthy persons.

During the prevalence of infantile paralysis, there constantly occur amongst the persons in the environment of a patient, cases showing only indistinct symptoms: fever, tiredness, nausea, headache, vomiting, somnolence, etc. but never pareses, such indisposition being often accompanied or followed by a certain irritability of temper. Sometimes symptoms are observed indicating a slight irritation of the central nervous system, such as stiffness of the neck, pains in the back of the head, in the dorsal and sacral regions and in the extremities, paraesthesiae, etc., the connection of the latter cases with infantile paralysis being most easily unveiled. At other times, disturbances of the digestive tract, such as vomiting and diarrhoea, predominate; in others, again, symptoms from the respiratory organs: nasal catarrh (possibly in combination with conjunctivitis or otitis media), angina, swelling of the tonsils and cervical glands. In such cases the connection with infantile paralysis is not so readily disclosed. As a rule health is restored very soon. WICKMAN has drawn attention to the connection between these atypical cases and the infantile paralysis and more especially to their importance as carriers of infection. He has called them *abortive cases*. There is no reason for assuming that these cases should appear only in the surroundings of patients showing typical pareses; on the contrary one is justified in assuming that they will occur without any distinct signs of paralysis presenting themselves in the patient. During the large epidemic in Sweden of last year, there were plenty of opportunities for observing such cases.



The only method hitherto known by which it could be determined whether such cases were caused by the virus of infantile paralysis, was to demonstrate in the blood after recovery from the illness, the presence of a bactericidal anti-body against the microbe of infantile paralysis. But for our purpose it would no doubt be sufficient to prove the presence of the microbe in the secretions by means of an inoculation into monkeys. We have made an investigation with regard to this point on a number of cases. In the following account they are divided into two sections: *cases of slight illness in persons having had contact with cases of infantile paralysis showing distinct pareses and cases where no such intercourse could be traced.* We have, besides, examined a number of *healthy persons living in the surroundings of those attacked by infantile paralysis.*

The washing-operation, and the inoculation of the monkeys have here been performed in the same manner as previously described.

*A. Cases without pareses in contact with cases of infantile paralysis presenting distinct pareses.*

#### Observation I.

*Family A.*, consisting of 5 members. 1) *The father*, and 2) *the mother*, were not affected.

3) *The son Åke*, 3½ years of age, had been fretful since the beginning of November, was taken ill, on Nov. 16, with headache, vomiting and general weakness, was dull and sleepy. On Nov. 18 and the day following, he was occasionally raving, mostly during the night. On Nov. 20 he was admitted to Kronprinsessan Lovisas Hospital for Children, tubercular meningitis being suspected. He was very drowsy with a staring and absent look, the pupils equal,

the neck somewhat stiff, he experienced pain on moving the head, and had possibly a slight left-sided facial paresis. On Nov. 23, the sensorium a little clearer, the stiffness of the neck gone, but in the evening a slight paresis of the arms was observed. Nov. 24, the sensorium still clearer, the paresis of the arms more marked, indistinct paresis of the ocular muscles, the patellar reflexes, present in the morning, were gone in the evening. Nov. 25, paresis of the right leg; was that same day transferred to the Epidemic Hospital of Stockholm.

The patient is somewhat drowsy and peevish, does not show any tenderness over the spine, the cervical muscles rather flaccid, shows marked paresis of the arms, even when lying down he can only with difficulty lift them, the right arm a little weaker than the left. He is unable to sit up in bed, the power of the legs diminished, but he can stand on them and walk with a support; the plantar, cremaster and abdominal reflexes normal, the Achillestendon reflexes absent, the patellar reflexes on the right side greatly reduced, normal on the left, the triceps reflexes normal on the right, reduced on the left side. The pharynx slightly reddened.

Dec. 4, the paresis of the arms much less marked, the patient now being able to lift them almost without hindrance, especially the right one; when attempt is made to make the patient sit up in bed he complains of great pain. Dec. 11, he can sit up in bed himself, experiences still some difficulty in raising the left arm, can walk with support, the gait, however, being stumbling and ataxic. Discharged Dec. 20.

4) *The girl Isa*, 8 years of age, onset Nov. 14 with fever, nausea and vomiting, remained in bed until Nov. 16 and was well after that.

5) *The boy Sven*, 5 years of age. Nov. 20, vomiting. Nov. 21, fever with delirium; after that well but irritable.

*The family B* had frequent contact with family A, especially during the middle of the autumn.

1) *The husband* was attacked on Nov. 7, with angina, pains and weakness of the legs. Remained in bed 4 days.

2) *The wife*, a sister of the above mentioned Mr. A., fell ill a week later with fever and symptoms like those of her husband. She had further pains in the back of the head and one half of the face. She stayed in bed two days.

3) *The daughter Maria Elisabeth*, 3 years of age, was attacked on Nov. 22 with a sore throat and difficulty in swallowing, after

having felt unwell for two or three weeks and grown thin and pale. The next day the throat was better, but she complained of pains in the knees, had fever and stiffness of the neck. Was admitted to the Epidemic Hospital on Nov. 24.

The general condition and nutrition good, the sensorium clear, does not complain of any pain, no stiffness of the neck, no tenderness over the spine, the head is not flaccid, no vomiting, no pareses of the arms, can easily sit up in bed, the motor power of the legs distinctly reduced, equally in both, all movements possible although performed with reduced strength. The patient is able to walk with support, but unsteadily, the knees easily giving way. The patellar reflexes are absent, the Achilles-tendon reflexes are diminished, other reflexes normal. The pharynx flushed.

Nov. 26. Yesterday and during the past night she had twitchings of the arms and head, the paresis of the legs has increased, she is now unable to stand on them. Dec. 1, the last few days rather marked tenderness of the legs, especially in the calves. Dec. 11, still considerable tenderness in the calves, the feet inclined to assume the position of plantar flexion. Dec. 20, the general condition good, the motor power of the legs still greatly reduced and the tenderness in the calves remains, she is able to stand on the right leg but not on the left one; the patellar reflexes absent; discharged.

4) *The daughter Ingeborg*, 10½ years of age, was taken ill with fever, headache and sore throat simultaneously with her sister.

Four children remained healthy.

On Nov. 25 washing of the mouth was performed on Mr. and Mrs. A. and on the boy Åke and the girl Isa. The filtered specimens were injected into monkeys, about 1,0 c. c. into one sciatic nerve and the rest into the peritoneum.

1) *Mr. A.*

Of the specimen from the *mouth*, 90 c. c. were, on Dec. 2, injected into *Macacus cynomolgus* no. 179. Dec. 13, hobbling along. Otherwise nothing abnormal was observed until Dec. 31, when the animal was found dying. Dead the same day.

The brain showed no marked changes. The superficial vessels of the spinal cord not distinctly marked, the section of the spinal cord slightly swollen, moist, the grey matter moderately greyish-

red. Microscopic examination: marked hyperaemia and solitary haemorrhages but no cellular infiltration, a few glia cells enlarged, clear, bright, the greater part of the nerve cells of the lumbar cord and some also of the other part of the spinal cord as well as of the medulla oblongata considerably degenerated with homogeneous, deeply stained and highly vacuolated, sometimes almost sponge-like protoplasm; in the medulla oblongata there remains of the nerve cells sometimes only small, radiating bodies.

*Macacus cynomolgus* no. 231 was inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord, on Jan. 8. It was observed for several months, but showed no symptoms of disease.

2) *Mrs. A.*

40 c. c. of the specimen from the *mouth* were injected into *Macacus cynomolgus* no. 187, on Dec. 9. This monkey remained in good health.

4) *Isa A.*

Of the specimen from the *mouth*, 100 c. c. were, on Dec. 2, injected into *Cercopithecus fuliginosus* no. 178. Dec. 12, does not climb willingly, runs slowly, is weak in the legs. Dec. 30, dead.

The brain shows no macroscopical change. The surface of the spinal cord rather pale, the section swollen in the lumbar and dorsal regions and the grey matter moderately greyish-red in colour. The middle lobe of the right lung contains a recent pneumonia. Microscopic examination: Intense hyperaemia, no haemorrhages and no cellular infiltration, a great number of the glia cells considerably enlarged, clear and transparent, in the spinal cord the majority of the ganglion cells are more or less changed, the nuclei being either very pale or not at all stained and the protoplasm homogeneous, deeply stained, intensely vacuolated or fenestrated, reminding of a sponge with large holes, the surrounding large, clear cells having, besides, eaten themselves so deeply into the nerve cells, that of these sometimes only star-like rests remain. In some places of the lumbar cord the cells of the anterior cornua are completely destroyed. Also in the medulla oblongata the nerve cells are to rather a great extent more or less changed.

*Macacus sinicus* no. 230 was, on Jan. 8, inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord. Febr. 20, walks and climbs slowly, is weak in all the extremities, is easily made to fall. Febr. 21, dead.



The surface of the brain much injected, that of the spinal cord rather less, the section of the spinal cord greatly swollen and the grey matter of a pale reddish colour. Microscopic examination: Distinct hyperaemia and in some places rather numerous, small haemorrhages but no cellular infiltration; the greater part of the glia cells more or less enlarged, clear and transparent; most of the nerve cells have undergone a change, the nucleus being shrunken, diffusely stained and the cell body either pale, finely granular as though liquified at the edge or else dark, shrunken and highly vacuolated, also sometimes deeply notched by the surrounding, large glia cells.

5) *Sven A.*

Of the specimen from the *mouth*, 100 c. c. were injected, on Dec. 9, into *Macacus rhesus* no. 186. On Jan. 18 the animal was found dead, nothing unusual having been previously observed.

The surface of the brain as well as that of the spinal cord rather pale, the section of the spinal cord does not swell, the grey matter in the enlargements of a slight greyish-red tint with distinct small, red spots. Advanced tuberculosis of the left, less advanced of the right lung, tubercles in the liver and spleen. Microscopic examination: Hyperaemia and small haemorrhages, but no cellular infiltration, the glia cells hardly changed; a rather great number of the ganglion cells deeply stained, shrunken and often considerably vacuolated; karyolysis.

The monkeys injected with the specimens obtained from the mouth of the father and the girl Isa, did not show any typical pareses, it is true, but a certain degree of weakness of the muscles was nevertheless observed. In the spinal cords cellular infiltrations and leucocyte-neuronophagias were missing, but on the other hand marked hyperaemia, considerable degeneration of the nerve cells and distinct changes of the neuroglia cells were found, i. e. changes similar to those previously observed in monkeys that have undoubtedly been affected by poliomyelitis. It is of itself improbable that the small recent pneumonia found in monkey no. 178 could have caused the far reaching changes in its

nervous system and, besides, the control inoculation has also proved, that the spinal cord contained an injurious agent capable of giving rise to similar changes. The investigations have thus proved that the buccal secretion of the slightly affected girl Isa as well as of her father who was perfectly well contained the microbe of infantile paralysis. With regard to the boy Sven it must remain unsettled, since we have not been able to decide, what part the advanced tuberculosis present in the monkey played in the origin of the changes described.

Of the five members of this family one has had infantile paralysis with clinically undeniable symptoms, two an uncertain illness of short duration and two, the oldest ones, remained well. The presence of the microbe of infantile paralysis could be demonstrated not only in one of the two who were slightly attacked, but also in one of those who remained well the whole time. *Of three individuals carrying the microbe of infantile paralysis on their mucous membranes only one has fallen ill with distinct pareses, one has been an abortive case and one a carrier of the virus.*

## Observation II.

*The family H.*, consisting of five members, comprising a servant girl of 19 years of age. The husband and the wife, both 37 years of age, as well as the servant girl, remained in good health.

1) *The girl Eva Maria H.*, 3 years old, was taken ill, on Oct. 12, with fever and restlessness. On Oct. 13 in the morning, she vomited, after that she stayed in bed, feeling tired and drowsy. Oct. 16, worse, has slept much, left arm weak, headache, bowels constipated.

Was on Oct. 18 admitted to the Epidemic Hospital of Stockholm. Drowsy and indifferent, does not complain of any pains, no stiffness of the neck, some tenderness over the spine; no paresis of the muscles of the neck, marked paresis of the left arm which she cannot be induced to move, the motility of the shoulder-joint evidently being especially reduced, whereas she is able to move the fore arm; no paresis of the right arm, slight paresis of the right leg; the patient is able to walk with support, but rather unsteadily, the right leg easily giving way. The reflexes of the left leg normal, on the right side the patellar reflexes lively, the Achilles-tendon reflexes reduced, the triceps reflexes normal. The pharynx slightly reddened.

Oct. 23, the gait still unsteady, cannot walk without support, is unable to lift the left arm. Nov. 5, walks rather well, drags the feet a little, still unable to lift the left arm. Nov. 12, the condition as before, the triceps reflexes reduced, the patellar reflexes normal. Nov. 20, discharged.

2) *Ingeborg H.*, 3 years. Was attacked, on Oct. 15, with cold shiverings and fever, restlessness, no headache, no vomiting.

Was admitted to the Epidemic Hospital of Stockholm on Oct. 18. Rather peevish and obstinate, no pains, no tenderness over the spine, no stiffness of the neck, no pareses, the gait normal, reflexes normal. Oct. 19, the patellar reflexes somewhat increased. Oct. 30, no objective signs, discharged.

On Oct. 19, washing of the mouth and intestine was performed on the girl *Ingeborg* the specimens were filtered and injected into monkeys into the peritoneum and sciatic nerves.

Of the specimen from the *mouth*, 100 c. c. were injected, on Nov. 17, into *Macacus rhesus* no. 156. No symptoms of disease were observed.

The *intestinal* specimen was injected into two monkeys. *Macacus cynomolgus* no. 131 was inoculated with 65 c. c., on Nov. 6. Nov. 11, does not run as lively as before; on climbing it finds it difficult to lift itself by the hands, no weakness of the legs perceptible. Was observed during a couple of months without showing any further symptoms of disease. — *Macacus rhesus* no. 130 was, on Nov. 6, inoculated with 130 c. c. of the same intestinal specimen. The animal remained well.

On Febr. 3, 1912, a second washing of the mouth and intestine of the girl Ingeborg was performed.

Of the specimen from the *mouth*, 140 c. c. were, on Febr. 5, injected into *Macacus cynomolgus* no. 249. Febr. 10, is lying on the bottom of the cage, moving only very little, dies in the afternoon.

The brain does not show any macroscopic changes. The vessels on the surface of the spinal cord moderately distended, the section not swollen, the grey matter well marked, and in the lumbar enlargement of a greyish-red colour. Microscopic examination: Hyperaemia and haemorrhages, but no distinct cellular infiltration nor enlargement of the glia cells; the greater number of the nerve cells changed, the nucleus shrunken, diffusely and generally slightly stained, the cell body shrunken, deeply stained, sometimes homogeneous and sometimes showing the tigroid substance rather well preserved; solitary nerve cells are hollowed out by the surrounding glia cells, the degeneration of the nerve cells being, as a rule, not very far advanced.

The *intestinal* specimen, 120 c. c. was, on Febr. 5, injected into *Cercopithecus sabaeus* no. 248. Febr. 12, likes to sit still on the bottom of the cage but can run and jump rather well; in the evening it is distinctly weak in both legs, but especially in the right one. Febr. 13, moves very slowly and cautiously, unable to rise fully on the hind legs, when walking it sometimes drags the tips of the toes. Febr. 14, cannot rise on the hind legs. Febr. 17, is sitting round-shouldered on the floor, does not want to move, falls down when trying to walk and gets up only with great difficulty, the patellar reflexes are present on both sides, but less lively than usually. Febr. 18, dead.

The pia mater of the brain and of the spinal cord rather congested, the substance of the brain hyperaemic, on section the spinal cord swollen, the grey matter being plainly red, especially in the lumbar region. Microscopic examination: Hyperaemia and solitary haemorrhages, possibly a slight degree of cellular infiltration in the grey matter, distinct hypertrophy of some of the glia cells, extensive degeneration of the majority of the ganglion cells which are exceedingly pale, finely granular or, more often, changed into irregular, vacuolated, homogeneous, deeply stained masses of protoplasm without any processes and provided with a shrunken, diffusely stained nucleus, solitary nerve cells being moderately hollowed out by the surrounding glia cells.



After injection with the specimens obtained at the first washing from the girl Ingeborg H. only one of the monkeys inoculated with the intestinal fluid exhibited any signs of illness, chiefly consisting in weakness of the arms. It, however, recovered. Quite different results were obtained with the new specimens taken after  $3\frac{1}{2}$  months. Both monkeys inoculated with these latter specimens died, the one after 15 days without any previously observed paresis, the other after 12 days, after having shown marked pareses, particularly in the hind legs. The microscopic examination showed considerable changes in the ganglion cells of that monkey which developed pareses, while less marked change was found in the other animal.

### Observation III.

*The family C.*, consisting of five members, 1) the father 40 years, 2) the mother 30, and three children. The family lived in Kiel until Dec. 23, 1911 and then they left for Stockholm, arriving on Dec. 24.

3) *The boy Torsten Robert*,  $3\frac{1}{2}$  years old, was well until November 1911. In the early part of that month he had fever, vomiting and constipation for a couple of days. A physician was consulted in Kiel, purgatives and diet was prescribed. The boy grew pale and thin, but did not stay in bed. On arriving in Stockholm, on the morning of Christmas Eve, having left Kiel the day before, he felt tired and slept a few hours in the forenoon. In the afternoon abdominal pains, enema. Dec. 26, pain in the abdomen, nausea and vomiting in the fore-noon which was repeated more frequently in the evening. The physician who was called observed that the vomited matter contained blood, the patient was unclear in his mind and crept about in bed, moaning and complaining of pains in the abdomen, vomited even after water, he was pale, respiration short and quick, dyspnoea, the pulse quick, no tenderness over the abdomen, no paralysis, crept about in bed moving the arms. He died the following day, Dec. 27.

At the post-mortem examination an intense hyperaemia of the brain and spinal cord was observed, on section the spinal cord was swollen, the grey matter was of a distinct greyish-red colour especially in the cervical region, the mesenteric glands swollen, otherwise nothing abnormal. The microscopic examination showed obvious hyperaemia of the spinal cord, no haemorrhages, no cellular infiltration; the ganglion cells slightly shrunken, as though somewhat too small for the spaces which they occupied but as a rule very little degenerated, the tigroid substance being mostly rather distinct, no neuronophagia. Vivid hyperaemia of the cortex of the brain.

A *Macacus rhesus* was inoculated with an emulsion of the spinal cord. It was found dead in the morning of the 24th day after inoculation, nothing unusual having been previously observed.

At the microscopic examination the following changes were found: Hyperaemia of the spinal cord, rather numerous, small haemorrhages, no cellular infiltration, hypertrophy of the glia cells, the ganglion cells as a rule deeply stained, often shrunken and, so to speak, hollowed out by the surrounding glia cells, here and there rather advanced neuronophagias.

4) *Harald Emanuel C.*, 2 years old, was attacked during the voyage with high fever, felt very hot, was better on arrival here, as also on Christmas-Day and the next day. On the third day he grew worse, commenced to cough, the cough lasting until the 30th, he had fever (38,0 C. in the morning and 38,5 C. at night), redness of the pharynx, nasal catarrh, but nothing from the lungs; no weakness of the arms or legs. Was sent to the Epidemic Hospital, on Dec. 30.

The general condition good, the mouth and pharynx normal, except that the tonsils were rather large; he coughs, a few râles are heard over the lungs, no stiffness of the neck, no tenderness in the back nor in the extremities, the gait normal, the patellar and other reflexes normal. Jan. 2, discharged.

5) *Fritiof C.*, 6 months old, onset on Dec. 31 with fever (38—39°), cough and nasal catarrh, the pharynx flushed. In the following week otitis media occurred.

Between Christmas and New year the *father* also felt rather feverish and indisposed.

The mouth and pharynx of the boy Harald were washed on Dec. 30 and the filtered specimen injected into the peritoneum and one sciatic nerve of a *Macacus*.

2) *Harald C.*

On Dec. 30, 45 c. c. of the specimen from the *mouth* were injected into *Macacus cynomolgus* no. 217. Jan. 2, somewhat weak in the left fore leg. Jan. 4, is mostly lying on the bottom of the cage, moves but very little, seems not to be able to rise on its hind legs; died in the evening.

The brain without any macroscopical change. The surface of the spinal cord is pale, on section the cord not swollen, the grey matter is, especially in the lumbar enlargement, rather reddish. Microscopic examination: Moderate hyperaemia, solitary, small haemorrhages, distinct hypertrophy of a large number of the glia cells especially around the nerve cells; in the cervical and the dorsal cords the majority of the ganglion cells are more or less degenerated, the nuclei being diffusely and slightly stained, some of the cells are shrunken, homogeneous, deeply stained, others pale, blueish, finely granular, the cells of the anterior horns sometimes being deeply infiltrated by the enlarged, surrounding glia cells, all that is left of the cells being then small star-shaped bodies.

*Cercopithecus fuliginosus* no. 232 was inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord. During the two months of observation it showed no symptoms of disease.

To make a definite diagnosis of the illness from which the boy Torsten Robert suffered was impossible during life. At the post-mortem examination, however, the intense hyperaemia of the nervous system, while changes in other organs were missing, gave rise to a suspicion of infantile paralysis, and this opinion was strengthened by the microscopic examination and confirmed by the experimental investigation on the animal. On account of the suspicion of infantile paralysis, the brother Harald was sent to the Epidemic Hospital, but in his case the illness did not develop into typical poliomyelitis. The monkey inoculated

with the specimen from his mouth was attacked on the 5th day with distinct weakness of the legs and died in the evening. The spinal cord of this monkey showed on microscopical examination widely spread, marked changes of the ganglion cells and hypertrophy of the glia cells. We have therefore considered ourselves justified in regarding this as an abortive case of infantile paralysis.

No doubt, the infection took place at Kiel, since the period of incubation of infantile paralysis is not, as far as is known, so short that there is reason to assume that the two elder boys had been infected in Sweden. According to information received from the medical Superintendent of the hospital for children in Kiel, professor v. STARCK, cases have occasionally appeared in Kiel since 1909—1910, during which latter year a larger number of cases of infantile paralysis occurred in the town and its surrounding county. The last case occurred on Dec. 1, 1911.

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Our attempts to demonstrate the presence of the microbe in the secretions from abortive cases have only comprised these three families. That these abortive types really are cases of infantile paralysis has been proved by the investigations of NETTER and LEVADITI, ANDERSSON and FROST and FLEXNER and CLARK, which have demonstrated the bacteriocidal influence exercised upon the virus of infantile paralysis by the serum from such cases. There is thus no reason to assume that these cases in any way differ from the typical cases in the question of the existence of the infectious agent.

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*A. Cases without pareses which, as far as could be ascertained, have not been in contact with cases of infantile paralysis showing distinct pareses.*

#### Observation IV.

*The family v. D.*, consisting of five members. The father Carl Gustaf, 38 years old, remaining healthy.

1) *The mother, Elisabet*, 32 years of age, complained during the illness of her daughters of tiredness, pains in the back of the head and a feeling of dizziness, when she tried to be out of bed. She had no fever during the whole time.

2) *Elisabet (Essy) v. D.*, 8 years of age, had, on Oct. 13, fever ( $39.6^{\circ}$  C.), nasal catarrh, the pharynx red and swollen but without any membranes, the culture not containing any diphtheria bacilli. Oct. 16, the temperature during the last few days  $37.8-38.2^{\circ}$  C., slight cough and nasal catarrh, excoriations around the nostrils, slight conjunctivitis, the pharynx slightly reddened, the tonsils enlarged, but no membranes. The lymphatic glands at the angles of the jaw swollen and tender, especially on the right side. Oct. 18, no fever, out of bed. Oct. 20, goes to school.

3) *Maude v. D.*, 7 years of age, was attacked, on Oct. 23, with fever ( $38.8^{\circ}$  C.) and nasal catarrh, very slight cough, redness of the pharynx but no swelling and no membrane. Oct. 24, the temperature  $38.6^{\circ}$  C., complained of earache, according to an ear specialist caused by an otitis med. cat. bilat. The next day better, no fever, could be out of bed.

4) *Kitty v. D.*, 10 months old, was attacked, on Oct. 10, with fever ( $38.4^{\circ}$  C.), nasal catarrh, redness of the pharynx, slight swelling of the cervical glands, the tympanic membranes red; the following day this redness had increased. Oct. 24, the patient had no fever, was bright and lively and the tympanic membranes were paler.

On Oct. 25 the mother's mouth and that of the girl Maude were washed, and about November 25 this was also done in the case of the other two girls. The filtered specimens were injected into the peritoneum and one sciatic nerve of monkeys.

1) *Mrs. v. D.*

On Oct. 27, 90 c. c. of the specimen from the *mouth* were injected into *Macacus rhesus* no. 102. The animal remained well.

3) *Maude v. D.*

On Oct. 25, 25 c. c. of the specimen from the *mouth* were injected into *Macacus cynomolgus* no. 103. Oct. 26, climbs slowly, runs joggingly. Oct. 28, still running badly, stumbles on the fore legs. In the afternoon it cannot be made to run, walks poorly, falls on the nose and seems to be weak in the hind legs. Oct. 29, dying; is killed.

The brain without macroscopic change other than the section was rather moist. The vessels on the surface of the spinal cord were only very little distended. The grey matter of the dorsal portion of the cord was of a pale red colour. Microscopic examination: Hyperaemia, but no haemorrhages, some ganglion cells slightly vacuolated, most of them, however, not presenting any changes worth mentioning, the tigroid substance being generally rather distinct.

*Macacus rhesus* no. III was inoculated, on Oct. 29, into one sciatic nerve with a non-filtered emulsion of the spinal cord and *Cercopithecus fuliginosus* no. 138 was inoculated, on Nov. 7.

No. III died suddenly on Dec. 27.

The pia of the brain rather markedly injected, a sharp contrast between cortex and medullary substance, both of which are richly spotted with blood. On section the spinal cord is swollen in the dorsal and lumbar regions and the grey matter is of a distinct greyish-red colour. In the left lung four caseous foci of the size of a bean are found and in the liver and spleen a few tubercles. Microscopic examination: Marked hyperaemia, no haemorrhages, solitary vessels in the medulla oblongata contain numerous leucocytes, possibly a slight cellular infiltration of the grey matter, very marked hypertrophy of the glia cells, degeneration of a great number of the nerve cells, which are retracted, homogeneous, deeply stained and vacuolated with shrunken, diffusely stained nuclei; the surrounding glia cells have penetrated far into the cells of the anterior horns, some of these being almost entirely eaten up.

No. 138. Nov. 9, jolts a little on the fore legs when running. Nov. 16, is still rather slow in its movements. Nov. 17, is very bad in the evening, sitting swaying the body, gait slow and very reeling, the animal sometimes falling towards the left, diarrhoea. A little

later it lies almost perfectly motionless, only moving the head very slightly but not the arms and legs, dies late in the evening. Moderate hyperaemia of the surface of the brain and spinal cord, the cerebral cortex being of a greyish-red colour. The section of the spinal cord is moist and greatly swollen and the grey matter is of a deep greyish-red colour. Microscopic examination: Intense hyperaemia in the medulla oblongata as well as in the entire spinal cord, oedema and solitary haemorrhages but no distinct cellular infiltration; hypertrophy of the glia cells; marked degeneration of the majority of the nerve cells, which are either shrunken, deeply stained with a homogeneous cell body that looks as if it was torn at the edges or else they are pale nearly dissolved or almost entirely disappeared, small striated or granular heaps being all that is left, the nuclei are shrunken, sometimes deeply and sometimes slightly, but always diffusely stained, into some of the nerve cells the surrounding glia cells have penetrated, though generally not very deeply.

2) *Essi v. D.*

*Macacus rhesus* no. 192 was, on Dec. 16, inoculated with 50 c. c. of the specimen from the *mouth*; remained well.

4) *Kitty v. D.*

*Macacus rhesus* no. 196 was, on Dec. 18, inoculated with 50 c. c. of the specimen from the *mouth*; remained well.

Only one of the monkeys inoculated with the specimens from this family became ill and it died. Some signs were presented that might be taken as symptomatic of an acute poliomyelitis, but on microscopic examination only very slight changes were found in the spinal cord. But two control animals which were inoculated with this spinal cord died, the one 60 and the other 10 days after the injection. The changes found in the spinal cords of these animals were much greater than those of the first monkey. One of the animals also showed clinical symptoms very similar to those of experimental poliomyelitis. This latter monkey showed no other changes that could explain the cause of death, while the other was affected with tubercle, though not to sufficient extent to be consi-

dered as a cause of death. Thus we have reason to assume that the latter two monkeys incurred poliomyelitis through inoculation of spinal cord from the first one. Consequently this original one must also have had poliomyelitis, and this in its turn shows that the girl harboured the microbe of infantile paralysis in her mouth and pharynx.

Thus only in the girl Maude did we succeed in demonstrating the presence of the virus. But all the members of the family, excepting the father, were simultaneously attacked by an acute febrile disease, and in one of them, the mother, signs of a slight irritation of the central nervous system were observed. Is it justifiable to assume that all these were cases of infantile paralysis? We believe so. It must be remembered that the washing of the two younger girls was not performed until about one month after their illness and that the inoculation of the specimens were, in consequence of want of animals deferred still another three weeks. It is therefore very possible that the virus during this time had become less virulent and so unable to infect the monkeys.

### Observation V.

*The family E.*, consisting of two members, a rather elderly woman and her adopted son *Julius*, a boy of 10.

In the morning of Oct. 31 the boy vomited before breakfast and felt ill all day. The next day he had headache and in the evening fever, 39.6° C. During the following days he still had headache and fever, about 38° C. in the mornings and somewhat higher in the evenings. On Nov. 4 temp. 40.1° C.; the physician who was called observed enlargement of the tonsils and redness of the pharynx; the patient looked tired and drowsy but had no pareses, no dyspnoea or cyanosis, no rash, nothing abnormal to be heard over



the lungs and heart, the patellar reflexes were normal and the pharyngeal specimen gave no diptheria bacilli. Nov. 6, no fever. Nov. 10, is pale, but otherwise nothing special. The mother was not ill.

On Nov. 10 washing of the *mouth* was performed on the boy.

The specimen, 95 c. c., was injected the same day into *Cercopithecus fuliginosus* no. 144. The monkey died on Dec. 19, nothing noteworthy having previously been observed.

The surface of the brain hyperaemic and the cortex here and there of a greyish-red colour. The surface of the spinal cord not markedly hyperaemic, the section swollen, especially in the lumbar region, the grey matter being distinctly reddish. In the upper lobe of the left lung a recent pneumonia. Microscopic examination: Hyperaemia, no haemorrhages and no cellular infiltration, the neuroglia cells to a large extent enlarged, clear, transparent; a great number of the ganglion cells, both in the medulla oblongata and spinal cord, more or less changed, with homogeneous protoplasm, sometimes shrunken, deeply stained and vacuolated, sometimes pale and with a small, irregular diffusely stained nucleus, no neuronophagias.

*Macacus rhesus* no. 207 was, on Dec. 21, inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord. Jan. 15, looks ill, respiration panting, climbs badly. Jan. 16, holds the right hand lifted when moving, but can use it when running and climbing. Jan. 17, very ill and in the evening was dead.

The surface as well as the substance of the brain hyperaemic, the vessels of the spinal cord moderately distended. On section the spinal cord not swollen and the grey matter but slightly reddish. A recent pneumonia in the upper lobe of the right lung and in the lower lobe of the left lung. Microscopic examination: Marked hyperaemia, scattered haemorrhages in the grey matter, but no cellular infiltration; a large number of the glia cells enlarged, clear, transparent; the ganglion cells present in some cases a fairly normal aspect with tigroid substance, but others show similar changes to those found in the preceding monkey. In addition, the surrounding glia cells have sometimes penetrated deeply into the cells of the anterior horns. These changes occur both in the medulla

oblongata and spinal cord, though perhaps they are more marked in the lumbar cord.

Although the monkey inoculated with the secretion from the mouth and which died after 39 days, did not exhibit any parietic symptoms, the microscopical changes were analogous to those usually found in the spinal cord of monkeys inoculated with secretion from abortive cases, changes we have reason to believe are due to the virus of infantile paralysis. No other cause of death could be found in this monkey. The control animal showed similar changes in the spinal cord, although they were less marked. These changes might perhaps be explained as caused by the recent pneumonia. But, on the other hand, the pneumonia might, with equal right, be assumed to be a result of the weakness of the respiratory muscles consequent upon the lesion in the neurons.

The boy harboured the virus of infantile paralysis in the secretions of his mouth and pharynx on the tenth day after the onset of an acute illness. One must naturally assume that the illness from which he had just recovered, and which was characterised only by swollen and red tonsils, fever, headache, nausea, but not by pareses, was due to this organism.

### Observation VI.

*Karl Oskar Harry F.*, 10 years old.

The boy was living in a district where a large number of persons had been attacked by infantile paralysis during the preceding autumn. He had been well up to Sept. 15, when he was suddenly attacked with nausea, vomiting and had to go to bed. He felt tired, seemed drowsy and yawned incessantly. The following day again repeated vomiting, even independent of the meals, drowsy and tired. No pain, no headache, no appetite. During the

following days he occasionally vomited, independently of the meals, his appetite was a little better but the bowels did not act. It was only on the eighth day, after an aperient, that the bowels moved freely, the motion having normal appearance. The temperature had not been taken at the onset of the illness. The constipation continued.

Was admitted to the Public Orphanage in Stockholm on Sept. 27. The first few days after admission he was rather drowsy, slept much, was cyanotic in lips and face. The frequency of the pulse varied, sometimes slow (66 per minute) and sometimes quick (120). Trousseau's line marked, no enlargement of the heart, the heart sounds normal. No action of the bowels without enema. Appetite now rather good. No pareses, no ataxia, no sensory disturbances. Marked disturbance of the speech, answers all questions hesitatingly and slowly. The temperature varying between  $37^{\circ}$  C. in the mornings and  $37.6^{\circ}$  C. in the evenings. The condition remained unchanged until Oct. 14. His bowels then moved spontaneously and after that he had an action of the bowels once a day. Heart-action now regular. Pulse 70—80 per minute. Bright and lively. Is discharged in full health on Nov. 29, 1911.

The symptoms presented by this patient: Vomiting independent of the meals, drowsiness, prolonged constipation, disturbance of the action of the heart, and Trousseau's cutaneous phenomenon, indicated an affection of the central nervous system, and as the patient had been attacked by an acute illness and came from a district, where infantile paralysis was common, the suspicion arose that the illness might be a form of infantile paralysis, and the Medical Superintendent, Prof. Medin, also considered this to be the most probable diagnosis.

On Oct. 31 the mouth of the boy was washed and the filtered specimen injected into the peritoneal cavity and one sciatic nerve of a monkey.

Of the specimen from the *mouth* 100 c. c. were, on Nov. 3, injected into *Macacus rhesus* no. 115. Nov. 22, climbs rather slowly, but runs pretty well. Dec. 8, still climbing slowly and jerkingly.

Dec. 11, climbs badly and with evident exertion, when jumping the legs are apt to give way. Dec. 12 in the afternoon, lies on the bottom of the cage, moves but very little. Dec. 13. Dead.

The pia mater of the brain markedly injected, that of the spinal cord pale. The section of the spinal cord very little swollen, the grey matter only slightly marked and very slightly reddish. Microscopic examination: Hyperaemia and haemorrhages but no certain cellular infiltration, hypertrophy of the glia cells, marked degeneration of the ganglion cells, of which some are pale, finely granular as if liquified at the edge, others shrunken, deeply stained, vacuolated and very often infiltrated by the surrounding, enlarged glia cells, sometimes being almost entirely consumed by them; the nucleus, usually small, diffusely and often deeply stained.

*Cercopithecus ruber* no. 204 was, on Dec. 20, injected with a non-filtered emulsion of the spinal cord into the peritoneum and one sciatic nerve. It died suddenly on the seventh day without any signs of paresis.

The superficial vessels of the brain very injected, the brain substance moist, more congested than normally, the contrast between cortex and medulla being sharp. The vessels on the surface of the spinal cord only slightly perceptible; the section of the spinal cord is moist, swollen and the grey matter, especially in the lumbar enlargement, is distinctly of a greyish-red colour. Microscopic examination: The spinal cord shows much the same changes as those found in the preceding monkey with the exception that the glia-cell-neuronophagias are less numerous.

The monkey inoculated with the secretion from the boy, developed 19 days after the inoculation symptoms which aroused a suspicion of poliomyelitis, but it did not die until 40 days after the infection. The changes present in the spinal cord were similar to those that have been found in several monkeys, the illness of which has been proved to be experimental poliomyelitis by inoculation of the spinal cord into control animals. The period of incubation, the symptoms and the pathological changes thus agreeing with what has been observed in monkeys attacked by poliomyelitis, we consider ourselves justified in making this diag-



nosis in the case of the monkey injected with the specimen from the mouth. The correctness of the diagnosis has been verified by the control inoculation in as much as the control animal showed similar changes in its spinal cord.

The presense of the micro-organism of infantile paralysis in the buccal cavity of the boy can thus be regarded as proved. But it goes without saying, that this does not prove that his illness was due to this organism, i. e. that his illness had been a form of infantile paralysis, though a rather uncommon one. It is to be remembered that the patient came from a district where at that time many cases of infantile paralysis had occurred. It is possible that the boy was simply a virus carrier and during that time contracted some other acute disease of unknown nature. In order to prove that his illness had been infantile paralysis the presence in his blood of a bactericidal antibody against the microbe of infantile paralysis needed to be demonstrated, and this we have not had an opportunity of doing. Anyhow, we consider it extremely probable that the illness from which the boy suffered was some form of infantile paralysis. If we should be mistaken as regards the diagnosis he must be considered a virus carrier. From an epidemiological point of view it is a matter of indifference wether the boy played the one or other rôle.

The existence of the micro-organism of infantile paralysis has thus been demonstrated *in the secretion from the mouths of three persons, who have not, as far as is known, had any contact with patients showing definite pareses, persons whose illness was characterized by such vague symptoms that only in one case did the suspicion*

arise that some form of anterior poliomyelitis was present. To arrive at this suspicion it required, however, the great and extensive experience of Prof. Medin. The two other patients had no symptoms reminding of typical cases of infantile paralysis, but in the family of one of them another member showed some symptoms that could be explained as signs of a slight cerebral irritation.

In addition to these three families we examined a few more, but with no positive result.

Once more we would point out that by demonstrating the presence of the virus in these persons, we have not proved that they have had infantile paralysis. Only the presence in the blood of a bactericidal anti-body to the virus of infantile paralysis is certain proof of this. The probability of the correctness of the diagnosis being, however, very great, and as a slight error in this respect would not lessen the value of the investigations, we have desisted from the attempt to demonstrate the presence of this anti-body, which procedure would very materially have added to our expenses.

*C. Perfectly healthy individuals in the surroundings of cases of infantile paralysis.*

#### Observation VII.

*The family G.*, consisting of four persons. The father and the mother had not been ill.

1) *The girl Lisen*, 1 year old, about Oct. 1 had a slight nasal catarrh. After that she remained well.

2) *Vanja Berta Elvira C.*, 7 years old, had been to school but the school became closed, cases of infantile paralysis having occurred amongst the pupils. She was attacked, on Oct. 17, with head-

ache, drowsiness and cold shiverings. Remained in bed on Oct. 19, suffering from pains in the left leg. On Oct. 20 and 21 she was out of bed at intervals, felt some weakness in the left leg, no headache during the last few days.

Was admitted to the Epidemic Hospital at Stockholm on Oct. 22. The mental condition clear, no pains, no stiffness of the neck, tenderness over the spine, the left pupil a trifle larger than the right, both reacting normally, slight lateral nystagmus, no paresis of the arms or trunk. The left leg slightly paretic; the right one normal, the patient can walk without support but with a slight limping in the left leg. The plantar and Achilles-tendon reflexes normal, the patellar reflexes somewhat reduced, the abdominal reflexes normal, triceps reflexes somewhat increased. The pharynx slightly reddened, no membranes. Oct. 30, walks with a slight limp in the left leg. Nov. 15, the general condition good, is still limping a little in the left leg, the patellar reflexes normal. Discharged.

On Oct. 26 the mouth of the girl Lisen was washed and the filtered specimen was inoculated on the same day into the abdominal cavity and one sciatic nerve of a monkey.

### 1) *Lisen G.*

Of the specimen from the *mouth* 95 c. c. were, on Oct. 26, injected into *Macacus rhesus* no. 106. Nov. 20, climbs slowly and jerkingly, is easy to catch, thin. Nov. 22, climbs very badly, tumbles on the nose when trying to jump, appears to be weak in the feet and runs slowly. Nov. 23, as previously. Nov. 25, dead.

The pia-arachnoid at the base of the brain vividly injected; similar change over the medulla oblongata and the cervical enlargement, but in other parts of the spinal cord they are pale. The section of the brain is moist and somewhat congested. The section of the spinal cord is not swollen, in the cervical region the grey matter is distinctly marked and of a slight reddish colour with solitary fine red dots. In the lower lobe of the left lung there is a caseous pneumonia, in the upper left lobe and in the right lung discrete miliary tubercles; tubercles also in the liver. Microscopic examination: Hyperaemia and haemorrhages but no cellular infiltration, hypertrophy of the glia cells, especially around the neurons; the nerve cells being to a large extent rather well preserved, the proto-

plasm rather homogeneous and more deeply stained than usually; some of the ganglion cells, especially in the dorsal and lumbar regions are distinctly degenerated and into some of them the surrounding glia cells have eaten their way.

*Cercopithecus fuliginosus* no. 174 was, on Nov. 29, inoculated into both sciatic nerves with a non-filtered emulsion of the spinal cord. Dec. 5, climbs with apparent difficulty, seems to be weak in all four limbs. Dec. 6. Dead.

The surface of the brain rather vividly injected and the contrast between cortex and medulla sharp. The surface of the spinal cord is also somewhat hyperaemic, the section greatly swollen and the grey matter everywhere of a pale greyish-red colour. Microscopic examination: Hyperaemia, haemorrhages and oedema, but no cellular infiltration, hypertrophy of a large number of the glia cells, especially in the lumbar region, the great majority of the nerve cells being shrunken, homogeneous, deeply stained, vacuolated and partly deeply infiltrated by the surrounding glia cells.

*Cercopithecus fuliginosus* no. 203 was inoculated, on Dec. 12, with a non-filtered emulsion of the spinal cord of the monkey no. 174. The injection was made into the peritoneal cavity and one sciatic nerve. Jan. 6, 1912, the animal is sitting crouched up on the bottom of the cage, moves unwillingly, slowly and with a limp, dragging the left hind leg; if pushed over, it is difficult for him to rise again. Jan. 7, dead.

The pia-arachnoid of the brain and spinal cord are rather vividly injected. The section of the spinal cord greatly swollen, the grey matter does not appear greyish-red. In the lower lobe of the left lung two patches of recent pneumonia, about the size of hazelnuts. Microscopic examination: Moderate hyperaemia in the medulla oblongata, no haemorrhages; hypertrophy of some of the glia cells of the spinal cord; the great majority of the nerve cells much changed, either very pale, finely granular or else shrunken, deeply stained, homogeneous and notched by the surrounding glia cells, the nuclei being small, irregular and as a rule diffusely and deeply stained.

The spinal cord of the monkey inoculated with the buccal specimen showed no marked change. In the control animal, on the other hand, the changes were much more marked and considerable changes of the ganglion



cells were found in the control to the latter monkey. All three animals exhibited evident pareses. There can therefore be scarcely any doubt that the animals had suffered from experimental poliomyelitis. Consequently the specimen from the mouth of the girl Lisen had contained the virus of infantile paralysis.

Most likely she had received the virus from her foster-sister, who in her turn probably was infected at school. There the latter had borrowed a book, which was not very clean. On the other hand it is not excluded that the contagion may have been transmitted in some other way. It is, however, hardly probable that the nasal catarrh from which the younger girl had suffered in the early part of October had anything to do with infantile paralysis.

### Observation VIII.

*The family I*, consisting of five members, including two servant girls.

In the early part of the summer, when infantile paralysis appeared in that part of Stockholm where the family lived, 1) the boy *Tom Erik*, 3 years old, was sent to a part of Skåne where no cases of infantile paralysis had then occurred nor did later on occur. As the cases increased in number in the neighbourhood of the house occupied by the family they moved, on Oct. 1, to another part of the town which was almost free from the epidemic. 2) *The father* and 3) *the servant girl Ellen N.* remained in town all the summer with the exception that the former passed his holidays during August in Skåne. 4) *The mother* passed most of the summer in Skåne but visited Stockholm a couple of times and remained there during the end of September to get ready for the removal. 5) *The servant girl Elsa J.* remained in Skåne with the boy the whole time. After the removal, the boy returned home in the middle of October. On Oct. 26 he was taken ill in the evening with vomiting and fever. On Oct. 27 in the morning, the general condition was bad,

he had fever ( $38.5-39.2^{\circ}$  C.), the patellar reflexes were increased on the right side, normal on the left; in the evening a slight attack of convulsions, and then gradually a distinct stiffness of the neck, twitchings of the muscles of the arm. Oct. 29, the patellar reflexes not increased. Oct. 30 in the morning, the patellar reflexes lost on the right leg, diminished on the left; in the evening absent on both legs. Oct. 31, the condition somewhat improved.

On Nov. 1 he was admitted to the Epidemic Hospital of Stockholm. The general condition rather good, but he is peevish and obstinate, not drowsy, marked stiffness of the neck but no tenderness on palpation of the spine as far as can be judged, marked flaccidity of the muscles of the neck, the power of the arms good, that of the legs somewhat reduced, especially on the right side. The patient can stand on his legs, which are held in the position of hyperextension, but he is unwilling to make attempts to move them forwards and then drags them along, the plantar reflexes normal on both legs; the Achilles-tendon and patellar reflexes on both sides distinctly reduced, cremaster and abdominal reflexes absent, the triceps reflexes normal, the pharynx normal.

Nov. 3, the general condition improved, perspires freely. Nov. 4, pains in both legs, the strength of the arms and legs as before, the patient can turn over in bed, no signs of tenderness on palpation but when the legs are lifted up he experiences pain. Nov. 5, he has during the night complained of pain in the back and legs, the pains do not, however, seem to have been so very intense, groans on palpation of the legs and upper arms, but is not tender over the spine, the flaccidity of the muscles of the neck diminished. Nov. 7, the general condition good, still some tenderness in the calves, is able to move the legs better than before. Nov. 8, can stand on his legs and walk short distances with support. Nov. 10, the power of the legs considerably increased, the tenderness of the calves almost entirely disappeared. Nov. 12, the condition still more improved, walks better, the patellar reflexes still considerably reduced. Nov. 17, the general condition good, no paresis of the muscles of the neck, arms or trunk, the strength of the legs, especially that of the left one, distinctly reduced, the patient can walk with support though somewhat unsteady, the knees easily giving way. The patellar, cremaster and triceps reflexes rather reduced, the plantar and abdominal reflexes normal; discharged.

On Nov. 2 a washing of the mouth and bowel was performed on Mr. I. and the servant girl Ellen N.

2) *Mr. I.*

The specimen from the *mouth* was injected partly into *Macacus rhesus* no. 125, which received 100 c. c., on Nov. 3 and partly into *Macacus cynomolgus* no. 136, which received 40 c. c., on Nov. 7.

No. 125 was found dead on Jan. 26, without having previously shown any signs of paralysis.

The surface of the brain and spinal cord pale, the section not swollen and the grey matter without any reddish tint. Tuberculosis of the lungs, though not very far advanced, isolated tubercles in the liver and spleen and a thin fibrinous coating over the inferior part of the lower lobe of the right lung. Microscopic examination: Hyperaemia and rather numerous haemorrhages but no cellular infiltration; the perivascular lymphspaces are, especially in the medulla oblongata, rather wide; the glia cells large, clear, transparent; the majority of the nerve cells are more or less changed, the nucleus in those of them that are best preserved having normal appearance, the cell body being homogeneous; a great number of the nerve cells are shrunken, deeply stained and vacuolated or else very pale and finely granular, the nucleus is small, diffusely and as a rule deeply stained, the hypertrophic glia cells have often deeply penetrated into the cells of the anterior horns; the changes are most pronounced in the lumbar cord.

No. 136. Nov. 8, runs and climbs somewhat slower than before and is easy to catch. Nov. 10, runs quicker, but still climbs slowly and with jerks. Jan. 5, still climbing slowly. Jan. 8, climbs exceedingly slowly, and with effort, shakes and trembles and holds the left hand in radial paresis-position, being, however, able to make use of it in grasping and climbing. Jan. 10, dead.

The brain shows no changes that are macroscopically perceptible. The surface of the spinal cord is pale, on section swollen and the grey matter somewhat greyish-red. The bronchial glands are caseous, miliary tubercles in the lungs, liver and peritoneum. Microscopic examination: Marked hyperaemia and numerous haemorrhages, accumulation of white corpuscles in the vessels but no definite cellular infiltration, hypertrophy of the glia cells, the majority of the nerve cells shrunken, homogeneous, deeply stained and some of them vacuolated; into most of them the surrounding cells

of the neuroglia have penetrated, reducing the neurons to small, irregular masses.

Of the specimen from the *intestine* 95 c. c. were on Nov. 6, injected into *Macacus cynomolgus* no. 133. Nov. 7, climbs slowly and with effort. Nov. 8, runs very slowly, limping and dragging the legs, when jumping the legs give way and the animal falls on its nose. Nov. 9, as before, but has marked paresis of the left hind leg, limps slowly along, attempts to climb but cannot raise itself. Nov. 10, all movements still slower and weaker, climbs and jumps with evident difficulty, is easily pushed over, slips sometimes when jumping or climbing, on a few occasions it has lost its hold with the hands, being able to hold on only with the feet. Nov. 11, seems at first to be rather lively but after a while it has hardly any strength to climb, seems to be especially weak in the hind legs; in the afternoon weak in all the extremities, jogs along with stooping back and with crooked knees, when walking the right fore leg is held outwards in an unnatural manner. Nov. 12, marked paralysis of the right hand, walks on the right knuckles, climbs with the greatest difficulty, tumbles down. In the evening the monkey is sitting swaying its head to and fro. Nov. 13, lies motionless on the bottom of the cage, taking a few breaths; is killed.

The surface of the brain rather pale, the vessels of the spinal cord also being only slightly injected. On section the spinal cord not swollen, the grey matter distinctly marked but not reddish, on the contrary, yellow. Microscopic examination: The spinal cord presents scarcely any definite changes, some of the cells of the anterior horns being, however, rather homogeneous, deeply stained and slightly vacuolated, others again showing a well preserved tigroid substance.

*Macacus rhesus* no. 153 was, on Nov. 16, inoculated into the peritoneal cavity and one sciatic nerve with a filtered emulsion of the spinal cord from the preceding monkey. Nov. 19, climbs rather slowly and with jerks. The same condition prevails until Nov. 30, when the animal climbs and walks very slowly, stepping with grave, slow steps, can not be made to run. Dec. 1, is to day lying on the bottom of the cage moving only very little, diarrhoea. Dying in the evening; is killed.

The surface of the brain pale, the pia mater of the spinal cord corresponding to the posterior surface of the lumbar enlargement somewhat injected. On section the spinal cord slightly swollen



in the dorsal region, the grey matter being here as well as in the cervical enlargement somewhat greyish-red. The microscopic examination shows only inconsiderable changes in the cervical and lumbar regions but in the dorsal region, on the other hand, hyperaemia, haemorrhages, hypertrophy of the glia cells and marked degeneration of the nerve cells, into which the surrounding enlarged, glia cells have deeply penetrated.

### 3) *Ellen N.*

Of the specimen from the *mouth* 60 c. c. were, on Nov. 7, injected into *Macacus cynomolgus* no. 135. Nov. 11, climbs a little slower than before and with jerks. Nov. 30, climbs to-day remarkably slowly, runs rather slowly too and is evidently weak in the hind legs, which are often dragged along. After walking a little while the animal drags plainly and constantly with the dorsal surface of the left foot on the ground at every step. Dec. 1, lying in a dying condition, died in the afternoon.

The brain has a normal appearance. The vessels on the surface of the spinal cord are rather distinctly marked, the section of the spinal cord not swollen, but moist and the grey matter has a distinct red colour with red spots. Microscopic examination: Intense hyperaemia and numerous haemorrhages in the grey as well as in the white matter, especially in the cervical region but also in the medulla oblongata, no cellular infiltration; the majority of the nerve cells have a dark, diffusely stained nucleus, the protoplasm being deeply stained, homogeneous and in some places also shrunken and vacuolated; the changes are as a rule not far advanced and only into a few of the nerve cells have glia cells penetrated.

*Macacus rhesus* no. 129 was, on Nov. 4, injected with 80 c. c. of the *intestinal* specimen and *Macacus cynomolgus* no. 134 with 95 c. c., on Nov. 6. The latter monkey showed no other symptoms than that during a short period, counted from Nov. 8, it did not run as quickly as previously.

No. 129. Nov. 27, climbs slowly, runs badly, dragging the hind legs, after a while it falls, being too weak to rise again, it lies still after that, hardly moving; the respiration superficial and quick. Nov. 28, dead.

Very marked hyperaemia of the pia of the brain and spinal cord. The cortex of a deep reddish tint, the whole substance of the brain being moister than usually and congested. The section of

the spinal cord is everywhere swollen and the grey matter has a marked reddish colour. Microscopic examination: Marked hyperaemia, haemorrhages in the medulla oblongata and in the spinal cord and here and there oedema; some of the glia cells, especially those surrounding the neurons and the vessels enlarged, clear, transparent (Fig. 5); the majority of the nerve cells much changed, especially in the lumbar region, some being homogeneous, shrunken, deformed and deeply stained, sometimes encroached upon by the surrounding glia cells and through them reduced to small, star-shaped bodies, others pale, as if dissolved, the nuclei shrunken, diffusely stained or entirely disappeared.

On Dec. 8 the father and the servant girl Ellen N. were again subjected to a washing of the mouth and intestine, and on the mother and the servant girl Elsa J. the same operation was also performed.

#### 2) *Mr. I.*

Of the *intestinal* specimen 120 c. c. were, on Dec. 20, injected into *Cercopithecus sabaeus* no. 202. Dec. 27, remains on the bottom of the cage, does not climb, is weak in all the extremities, runs slowly, dragging the hind legs, now and then tumbling on the nose, or falling to the side on the left hind leg. Dec. 28, is to day lying on the bottom of the cage almost motionless; is killed.

The surface of the brain, especially corresponding to the occipital lobes, intensely hyperaemic. The surface of the spinal cord, on the contrary, only slightly hyperaemic, the section of the spinal cord not swollen and the grey matter not red. Microscopic examination: In some places slight cellular infiltration of the pia, intense hyperaemia, solitary haemorrhages in the medulla oblongata, not quite distinct cellular infiltration in the spinal cord, the vessels containing, as a rule, numerous white corpuscles with sometimes an indication of cellular infiltration around them; hypertrophy of the glia cells; a good deal of the ganglion cells degenerated, homogeneous, shrunken and through invaded glia cells reduced to small, star-shaped bodies or else there remains of them nothing but a coarse net-work, the nuclei being either diffusely or not at all stained.

#### 4) *Mrs. I.*

Of the specimen from the *mouth* 70 c. c. were, on Dec. 21, injected into *Macacus rhesus* no. 205. The monkey died the following day of a bacterial peritonitis.

3) *Ellen N.*

Of the specimen from the *mouth* 115 c. c. were, on Dec. 22, injected into *Cercopithecus sabaeus* no. 210. Dec. 26, paresis of the right arm, the animal all the same trying to grasp with the hand. Dec. 27, is sitting with curved back, moving but very little and slowly, if pushed over it cannot get up; dead in the evening.

The brain of ordinary appearance. The vessels on the surface of the brain are everywhere highly distended, on section the spinal cord is not swollen but moist and the grey matter has a slight reddish tint. Microscopic examination shows marked hyperaemia and haemorrhages in the grey matter but no cellular infiltration; only a few of the glia cells are enlarged; some of the nerve cells are deeply stained, shrunken and vacuolated, others finely granular and disintegrated.

The specimen from the *intestine*, 95 c. c., was injected, on Dec. 22 into *Cercopithecus ruber* no. 209. Dec. 27, sitting stooping, walks staggeringly and unsteadily, on attempting to run it falls on its nose. In the afternoon the condition the same. Dec. 28, dead. The monkey had the whole time been alone in a cage that had previously been cleaned.

The brain without any distinct changes. The vessels of the spinal cord not especially pronounced. The section of the spinal cord not swollen, the grey matter only slightly marked but somewhat spotted with red at the commissure. The greater part of the lower lobe of the right lung occupied by a recent pneumonia. Microscopic examination: Hyperaemia and haemorrhages but no cellular infiltration; the glia cells enlarged, clear, transparent; a great number of the nerve cells being shrunken, deeply stained, vacuolated, the enlarged glia cells having sometimes eaten their way into them.

*Cercopithecus Burnetti* no. 223 was, on Jan. 2, inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord of the foregoing monkey, and *Macacus cynomolgus* no. 236 with a filtered emulsion both into one sciatic nerve and the peritoneal cavity, on Jan. 12.

No. 223 was found dead on Jan. 7.

The surface of the brain and dorsal aspect of the spinal cord much injected. On section the spinal cord slightly swollen, the margin of the grey matter being indistinctly marked and only in

the dorsal region of a light reddish colour. On microscopical examination the spinal cord showed much the same changes as those found in the preceding monkey, though perhaps somewhat more marked.

No. 236. Febr. 13, climbs slowly and is evidently weak in both hind legs. Febr. 17, the weakness of the hind legs increased, the animal walking badly, reeling and falling. Febr. 18, paralysis of the right foot, paresis of the rest of the leg. Febr. 19, walks very slowly, crosses the hind legs and staggers to and fro, the legs now and then giving way, causing the animal to fall, the patellar reflexes weaker on the right side than on the left. Febr. 20, dead.

The superficial vessels of the brain are very injected, a sharp contrast noticeable between the cerebral cortex and the medullary substance. The surface of the spinal cord is pale; the section not swollen and the grey matter not reddish. The bronchial glands caseous, no tuberculosis of the lungs but tubercles in the liver and the spleen. Microscopic examination: Slight hyperaemia, scattered haemorrhages but no marked cellular infiltration, hypertrophy of the glia cells around the neurons; a great number of the nerve cells much changed, transformed into irregular or star-shaped, homogeneous, deeply stained lumps of protoplasm, the nucleus being diffusedly or not at all stained; the surrounding glia cells have penetrated deeply into the degenerated ganglion cells.

### 5) *Elsa J.*

The specimen from the *mouth*, 80 c. c., was, on Dec. 22, injected into *Cercopithecus Burnetti* no. 208. Dec. 23, is lying on the bottom of the cage, moves only very slightly, slowly and hesitatingly, the joints not flaccid, slight strabismus convergens. Dec. 25, dead. The monkey had the whole time been alone in a previously cleaned and disinfected cage.

The surface of the brain pale, that of the spinal cord, on the other hand, slightly injected on the ventral surface, the section of the spinal cord much swollen. The microscopic examination shows hyperaemia and a considerable oedema, intense degeneration of the nerve cells, of which there remain as a rule nothing but small torn, homogeneous, deeply stained and sometimes vacuolated lumps of protoplasm, a few neuronophagias visible.

*Cercopithecus fuliginosus* no. 221 was, on Jan. 3, 1912, inoculated with a non-filtered emulsion of the spinal cord into one sciatic



nerve. Jan. 22, the monkey lies on the bottom of the cage, can scarcely move the legs but tries to get up on the arms. Jan. 23, dead.

Rather marked vascular injection of the surface of the brain, the cortex being fairly dark. The spinal cord is firm, not swollen on section, and the grey matter is hardly greyish-red. Microscopic examination: Considerable hyperaemia of the grey matter, scattered haemorrhages but no cellular infiltration; the majority of the glia cells enlarged, clear, transparent; a great number of the nerve cells are shrunken, deeply stained, homogeneous and vacuolated or else very pale and finely granular; the nuclei are diffusely and often slightly stained, some of the cells of the anterior horns being invaded by the surrounding glia cells. On the whole the changes are not very marked.

Of the *intestinal* specimen 110 c. c. were injected into *Cercopithecus sabaeus* no. 201, on Dec. 20. The monkey was found dead on Dec. 25, nothing unusual having previously been observed.

The surface of the brain slightly injected, the spinal cord on the other hand, especially on the posterior surface, much injected. The section of the spinal cord is markedly swollen. Microscopic examination shows hyperaemia and oedema as well as an accumulation of white corpuscles in the vessels but no cellular infiltration; there is hypertrophy of the glia cells and degeneration of the nerve cells, which are deeply stained, shrunken and homogeneous.

*Cercopithecus fuliginosus* no. 222 was, on Jan. 3, inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord. Febr. 8, the monkey is very thin and looks tired, climbs and walks with difficulty, falls easily. In the evening it climbs remarkably bad, is weak in both hind legs, more especially in the right one, the patellar reflexes are absent on the right and weak on the left side. Febr. 9, dead.

The superficial vessels of the brain vividly injected, a marked contrast noticeable between cortex and medulla. The vessels of the spinal cord are also somewhat injected and the grey matter is everywhere, though more especially in the cervical cord, of a marked greyish-red colour with fine red spots. Microscopic examination: Considerable hyperaemia and rather numerous haemorrhages but no cellular infiltration, hypertrophy of some of the glia cells around the neurons; the nerve cells degenerated as in the preceding cord, some of them being invaded by glia cells, though not deeply.

Two of the monkeys employed for the investigations on Mr. I. were, to our regret, attacked by tuberculosis. This circumstance might, needless to say, have had some influence on the result. Still, there seems no reason to doubt that the father also at the time when the first washing was done was a virus carrier. It is improbable that the tuberculosis was the cause of the degeneration of the ganglion cells. On the other hand, that he harboured the microbe when the last washing was performed, seems to us to be unmistakably proved by the investigation of the fluid obtained at the washing. The monkey inoculated with this specimen showed symptoms that were almost quite typical of experimental poliomyelitis. The monkey inoculated with the specimen from Mrs. I. died of peritonitis. Whether she was a virus carrier or not must remain undecided. With regard to the servant girls there seems to be no doubt that the monkeys inoculated with the respective specimen really developed poliomyelitis, when the clinical symptoms as well as the pathological changes are taken into consideration, and also the fact that the control animals after inoculation of their spinal cords died with marked changes in the nervous system, while macroscopical changes of the other internal organs were, on the other hand, absent. *Of the five members of the family, one has been suffering from infantile paralysis but, besides this, three other members have carried the virus without ever having been ill, i. e. we have found three »virus carriers» to one case of illness.*

With regard to the manner in which the contagion has been transmitted nothing can be said with certainty. It seems most probable, however, that either the father or the servant girl Ellen N., or both, had caught

the virus in Stockholm during the summer and that the boy was infected by them after his return home. The period of incubation seems also to favour this view. But it is impossible to exclude that he may have been infected elsewhere and that he in his turn transferred the microbe to the others. This, however, is for our purpose of quite a minor importance.

### Observation IX.

*The family K.*, consisting of eight members, viz.

- |   |                 |
|---|-----------------|
| 1) <i>Carl Viktor K.</i> , 34 years old, the father |                 |
| 2) <i>Agnes K.</i> , 43 years old, the mother       |                 |
| 3) <i>Maria Elisabet K.</i> , 15 years old,         | } the children. |
| 4) <i>Frans Oskar K.</i> , 13 » »                   |                 |
| 5) <i>Nils Gustaf K.</i> , 12 » »                   |                 |
| 6) <i>Julius K.</i> , 7 » »                         |                 |
| 7) <i>Ernst K.</i> , 4 » »                          |                 |
| 8) <i>Karin Elisabet H.</i> , 9 months.             |                 |

The neighbourhood in which the family lived is very isolated and no case of infantile paralysis had previously occurred there. None of the members of this family had for a long time before Oct. 19 left their home at which date the *father* and the *boy Ernst* visited Stockholm in order to consult a physician about the enlarged tonsils of the boy. These are said to have been excised.

About Nov. 14, *Ernst* knocked himself against a door; soon after that the parents noticed that his left leg seemed stiff and that he could only move it with difficulty, helping it with the hand. On Nov. 16, in the evening, he had headache and was tender all over the body. During the night of Nov. 19 temp. 39.9° C., intense headache and twittings, especially in the left arm and leg as well as in the face. Nov. 23, very tender all over the body, the head bent backwards, cannot sit up, if made to sit up in bed he falls, complete paralysis of the right arm, marked paresis of the left one, complete paralysis of both lower extremities. Patellar and abdominal reflexes absent. No constipation.

The boy *Julius* suffered from headache and vomiting on Nov. 17, stayd in bed half of the next day, but after that remained well.

On Nov. 23 washing of the mouth and the intestine was performed on the members of the family excepting the boys Ernst and Julius and the girl Karin Elisabet.

1) *Carl Viktor K.*

The specimen from the *mouth*, 95 c. c., was injected into *Macacus rhesus* no. 171, on Nov. 27. The animal seemed to be in good health for two months but died of tuberculosis about three months after the inoculation.

The specimen from the *intestine*, 150 c. c., was, on Nov. 25, injected into *Cercopithecus Burnetti* no. 170. The animal died on Dec. 8, nothing remarkable having been observed during the last few days.

The pia of the brain vividly injected, the spinal cord pale on the surface. The section of the spinal cord only very slightly swollen, but the grey matter everywhere of a greyish-red colour with fine red spots. Microscopic examination: Marked hyperaemia and numerous haemorrhages, some of them rather large, no definite cellular infiltration but in some places a layer of cells arranged in one row around the middle-sized vessels of the grey matter; the glia cells large, clear, pale; the ganglion cells shrunken, deeply stained and vacuolated, the nuclei diffusely and slightly stained or else apparently disintegrated; into some of the cells of the anterior horns the glia cells have eaten their way but, as a rule, not very deeply.

*Macacus rhesus* no. 191 was, on Dec. 15, inoculated into one sciatic nerve with a filtered emulsion of the spinal cord. Jan. 1, is sitting on the bottom of the cage crouching, dying later in the day.

The brain without macroscopical changes, the spinal cord pale on the surface. The section not swollen and the grey matter only in the lumbar region of a slight greyish-red colour. Microscopic examination: Hyperaemia, a few haemorrhages, hypertrophy of the glia cells and degeneration of a great number of the nerve cells in appearance about the same as in the preceding spinal cord; the glia cells having often penetrated far into the cells of the anterior horns.

2) *Agnes K.*

Of the specimen from the *mouth* 105 c. c. were, on Nov. 29, inoculated into *Cercopithecus fuliginosus* no. 173. Nov. 30, climbs



with jerks. Dec. 2, lying almost motionless on the bottom of the cage; is killed.

The superficial vessels of the brain moderately filled with blood, the surface of the spinal cord pale. Over the apex of the right occipital lobe a haemorrhage in the pia of the size of a pea, on section the spinal cord swollen in the dorsal region, the grey matter hardly of a reddish tint. The microscopic examination shows hyperaemia, scattered, small haemorrhages, no cellular infiltration, no hypertrophy of the glia cells, the nerve cells being only slightly changed, no neuronophagias.

The *intestinal* specimen, 100 c. c., was injected into *Macacus rhesus* no. 172, on Nov. 27. The animal remained in good health.

### 3) *Maria Etisabet K.*

The specimen from the *mouth*, 100 c. c., was injected, on Nov. 24, into *Macacus rhesus* no. 169, but without giving rise to any symptoms of disease.

The *intestinal* specimen, 100 c. c., was the same day inoculated into *Macacus rhesus* no. 168. This monkey remained in good health.

### 4) *Frans Oskar K.*

*Macacus rhesus* no. 167 was, on Nov. 24, injected with 125 c. c. of the *buccal* specimen. Dec. 28, dead.

The region behind the left ear and the left half of the face a good deal swollen. Any special cause for it could, however, not be found at the post-mortem examination. The surface of the brain moderately hyperaemic, the cortex in some places of a rather vivid red colour. The surface of the spinal cord slightly hyperaemic, the section not swollen, the grey matter being well marked and in the posterior cornua possibly somewhat reddish. The lungs are hyperaemic, slightly oedematous. Microscopic examination: Moderate hyperaemia and solitary haemorrhages in the grey matter, distinct cellular infiltration of the pia, also with polymorphonuclear leucocytes, the changes being most marked in the lumbar region; hypertrophy of the glia cells; degeneration of a great number of the ganglion cells which are shrunken, deeply stained, homogeneous and vacuolated; karyolysis; into some of the nerve cells enlarged glia cells have eaten their way. After staining for bacteria solitary Gram-positive diplococci were found in the pia.

*Macacus cynomolgus* no. 220 was, on Jan. 2, inoculated into one sciatic nerve with a non-filtered emulsion of the spinal cord.

Febr. 7, does not climb, cannot hold itself fast by the arms, attempts to walk but falls on the nose, paresis of the left hand. Febr. 8, dead.

Rather a vivid injection of the surface of the brain, fairly sharp contrast between the medullary substance and the cortex. The surface of the spinal cord is pale and the section not swollen, the grey matter not reddish. Microscopic examination shows marked hyperaemia, numerous haemorrhages, degeneration and neurophagia of the ganglion cells as in the preceding spinal cord.

The *intestinal* specimen, 130 c. c., was injected, on Nov. 24, into *Macacus rhesus* no. 166. This monkey remained well.

### 5) *Nils Gustaf K.*

The specimen obtained from the *mouth*, 100 c. c., was, on Nov. 24, injected into *Macacus rhesus* no. 164. Dec. 2, does not climb as quickly as before. Dec. 16, climbs with exertion and unnaturally, is possibly weak in the left hind leg. Dec. 19, is mostly sitting on the bottom of the cage, climbs badly, runs with a limp, dies in the evening.

The pia of the brain vividly injected, a marked contrast noticeable between the cortex and the medulla. The vessels of the spinal cord also somewhat injected, the section scarcely swollen but the grey matter rather markedly reddish, especially in the lumbar region. Microscopic examination: Hyperaemia and haemorrhages, especially in the commissure and its vicinity, no quite definite cellular infiltration, slight hypertrophy of a small number of the glia cells in the medulla oblongata and in the spinal cord; some of the nerve cells well preserved but a great number changed, shrunken, homogeneous, vacuolated, torn at the edges and deeply stained or in other cases of a pale bluish tint, extremely finely granulated; the nucleus diffusely and usually deeply stained, a few ganglion cells being somewhat infiltrated by glia cells.

*Macacus rhesus* no. 212 was, on Dec. 23, inoculated into both sciatic nerves with a non-filtered emulsion of the spinal cord. Jan. 8, thin, climbs and moves slowly and with exertion, groans. Jan. 9, dead.

The post-mortem examination shows a double-sided fibrinous pleurisy and a pneumonia in the right, lower lobe.

Of the *intestinal* specimen 90 c. c. were, on Nov. 24, injected into *Macacus rhesus* no. 165. Jan. 32, respiration laboured. Jan. 26, dead.

At the post-mortem examination it was found that almost the

whole of the left lung was occupied by caseous pneumonias, besides which tubercles were found in the right lung, the liver and the spleen.

In this family, which presented one typical and one abortive case of poliomyelitis, three virus carriers were discovered through the experiments on monkeys, viz. the father and the two elder boys. The monkey inoculated with the intestinal specimen from Frans Oskar developed, it is true, a leptomeningitis, but this was so slight that it was not discovered at the autopsy but only at the microscopical examination, and it could not have caused the considerable degenerations of the ganglion cells which were found to be present. Moreover, the control monkey died with similar changes without any mixed infection. Whether the mother was a virus carrier also cannot be concluded from the experiments, but this is very probable as she nursed the boy during his illness. The changes found in the monkey which had been inoculated with the specimen from the mother, were rather insignificant and its control animal remained well. As no other cause of death was discovered, and as the specimens from several other members of the family had caused poliomyelitis it is not unlikely that also this monkey was attacked by poliomyelitis.

Regarding the manner in which the infection was transmitted to the family it may be remarked, that on Oct. 24 a family from Småland came to live in the neighbourhood. At the place where this latter family had previously been staying neighbours had been attacked by infantile paralysis in September. The new family, however, did not live in the same house nor in the immediate proximity to the family K. It may also be suspected that the infection was caught during the visit to Stock-

holm paid by the father and the boy Ernst, this town being at that time the only place in the vicinity where cases of infantile paralysis had occurred. But on the other hand it cannot be decided whether it was the father or the boy or both who had acquired the contagion. One would perhaps be inclined to suppose that the operation performed on the boy might have predisposed him to the infection, and consequently in the first place to suspect the boy of being the conveyor of the disease. But on the other hand it must be remembered that the boys Ernst and Julius were attacked simultaneously. This does not exclude, however, that the latter was infected by the former, but considering the relative length of time which in such case the period of incubation would have lasted for Ernst, it seems more probable that both the boys were infected by the father. The family was isolated and no other cases occurred in the same parish.

### Observation X.

*The family L.*, consisting of five members: 1) *The father*, 2) *the mother and three boys*, varying in age from 14 to 19 years.

3) *Torsten*, 19 years old, clerk in a factory near Stockholm where no cases of infantile paralysis had occurred. He was living with his parents in Stockholm. Was attacked, on Nov. 13, with fever, indisposition and headache. Nov. 15 and 16, 3—4 attacks of vomiting lasting for about half an hour each time, pains in the legs with a sensation of creeping, pricking and numbness. On Nov. 17 the patient noticed that the right leg was somewhat weaker than the left. The condition during the next few days unaltered.

Was admitted to the Epidemic Hospital of Stockholm on Nov. 20. The general condition good, no stiffness of the neck, on bending the head forwards a slight pain is felt in the small of the back. No tenderness over the spine, the motor power of the trunk and arms



call for no remark, the power of the left leg normal, of the right one rather reduced, the patient limps a little in the right leg which is held slightly hyperextended. The plantar and patellar reflexes on both sides rather lively. The Achilles-tendon reflex on the left leg normal, absent on the right. The cremaster, abdominal and triceps reflexes normal. Nov. 24, slight pain in the small of the back off and on. Nov. 26, pains in the right gluteal region, tenderness over the sciatic nerve. Dec. 3, the pain in the gluteal region gone. Dec. 18, the movements of the right knee- and hip-joints take place with almost normal strength, but the patient cannot, when standing, rise on the toes of the right foot, the gait slightly limping, the patellar and Achilles-tendon reflexes normal; is discharged.

4) *Gösta L.*, 14 years old, had remained well during the whole time. Together with a friend Å. of his he used to take part in the scouting exercises and they used to meet every Sunday. Both served as patrol leaders and passed the nights near to each other. This was also the case on Sunday, Sept. 17, the last time they met, when they and their patrols had their sleeping places only at a few meters' distance from each other. The following day the boy Å. was attacked by infantile paralysis.

5) The *third brother*, a boy of 17, did not get ill.

On Nov. 30 a washing of the mouth and intestine was performed on Gösta L. After filtration through a Heim the specimens were injected into the peritoneum and the sciatic nerves of two monkeys.

4) *Gösta L.*

The specimen from the *mouth*, 100 c. c., was, on Dec. 1, injected into *Cercopithecus fuliginosus* no. 177. On Dec. 11 the monkey was found dead, nothing unusual having been observed during life.

Moderate hyperaemia of the surface of the pia; the cerebral cortex here and there of a reddish colour.

The superficial vessels of the spinal cord well marked, especially over the enlargements. On section the spinal cord is moist, greatly swollen and the grey matter distinctly marked, reddish. In the lower lobe of the left lung there is a small, recent pneumonia. Microscopic examination: Considerable hyperaemia and scattered haemorrhages but no cellular infiltration; the glia cells enlarged, clear, transparent; a great number of the nerve cells changed, either slightly stained

and as if broken up or dissolved or else shrunken, homogeneous, vacuolated and deeply stained with small diffusely and generally deeply stained nuclei, solitary glia cells having eaten their way deeply into some of the cells of the anterior horns. The changes are most pronounced in the lumbar cord, the cells of the lateral horns being better preserved, but even these are not wholly normal.

*Cercopithecus fuliginosus* no. 206 was, on Dec. 31, inoculated with a filtered emulsion of the spinal cord intraperitoneally and into one sciatic nerve. It remained well.

The *intestinal* specimen, 160 c. c., was, on Dec. 14, injected into *Macacus rhesus* no. 188. Dec. 21, looks bad, is rocking to and fro. On running a distinct weakness of the hind legs is apparent, causing the animal to fall. After a while the monkey cannot run at all, is only able to walk and that very unsteadily, reeling on the hind legs. In the evening complete paralysis of both hind legs, distinct paresis also of the arms, the animal trying to get up by their aid but immediately falling down. Dec. 22, dead. The animal had during the whole thime been isolated in a cage which had previously been cleaned and disinfected with lysol.

The pia of the brain and dorsal surface of the spinal cord vividly injected. A sharp contrast between the cortex and the medulla of the brain. The section of the spinal cord not swollen, the grey matter of a pale greyish-red colour in the cervical and lumbar enlargements. Microscopic examination: Hyperaemia and haemorrhages, but no definite cellular infiltration; the majority of the glia cells much enlarged, pale, transparent; the main part of the nerve cells in both the medulla oblongata and the spinal cord, chiefly perhaps in the lumbar region, are markedly changed, deeply stained, homogeneous and vacuolated with diffusely and generally deeply stained nuclei. Into many of the cells of the anterior horns the surrounding glia cells have penetrated very deeply, thus reducing the nerve cells to small, irregular masses (see Fig. 6 and 7).

Both monkeys showed marked changes in the spinal cord, wich we must consider as the cause of death, changes of other organs being absent that might be regarded as such with the exception of the small pneumonia in the monkey no. 177. The changes in the ganglion cells and the duration of the period of incubation correspond

also to what has been found in experimental poliomyelitis. And finally one of the monkeys presented quite a definite paralysis of the hind legs. There can therefore hardly be any doubt that the injected specimens from Gösta L. gave rise to poliomyelitis in the animals employed for the experiment. The boy must therefore have harboured the virus of infantile paralysis on his mucuous membranes although he had not been ill himself.

The question naturally arises whether he transmitted the disease from his friend Å. to his brother Torsten, who, as far as could be ascertained, had not had any communication with persons attacked by infantile paralysis. This seems very probable, though impossible to prove. It is just as possible that the boy Gösta had received the microbe from his brother, who may have contracted the disease elsewhere.

### Observation XI.

*The family M.* from Linköping, consisting of three members and one lodger.

1) *Axel M.*, 33 years old, a parcel-van-driver, caught some day after May 27 a cold, which continued for some time. He had also a slight cough but went on with his ordinary work and states that he did not feel ill.

2) *The wife, Hilda M.*, 31 years old, remained well during the whole time, excepting that she, like her husband, but somewhat earlier than he, had been suffering from a nasal catarrh, from which she had been troubled repeatedly during the spring.

3) *The son, John Arvid M.*, 9 years old, got headache on June 4 and remained in bed for a few days. At the same time he had a nasal catarrh but no stiffness of the neck was observed.

4) *Jenny Sofia A.*, 21 years old, a dressmaker, lived with the family. She had been at her home in the country during Whitsuntide, May 26—27. On returning to town on May 28 she felt ill,

had headache and a nasal catarrh. Notwithstanding this she kept working daily in her work-room until June 6 in the evening, when she had to remain in bed. No pareses were observed, however, until in the morning of June 8. She died the same day in the evening.

5) *The dressmaker Agnes J.*, 21 years old, worked in the same room as the preceding but lived elsewhere. She was also suffering from headache and nasal catarrh in the beginning of June.

On June 10 specimens of the buccal and pharyngeal secretions of the members of the family M. were taken in this way, that the mouth and pharynx were wiped out with sterile cotton swabs, which were afterwards washed in a sterile saline solution. They were also made to gargle themselves with saline solution, both fluids being then added together. A specimen from the dressmaker Agnes J. was taken in the same manner, on June 12. After filtration through a Heim the specimens were injected into monkeys.

#### 1) *Axel M.*

The specimen obtained from the *mouth*, 80 c. c., was on June 20, injected into *Macacus rhesus* no. 283. July 6, is sitting with curved back, does not want to walk and cannot be induced to climb, now and then the animal lies down on the bottom of the cage, and finds some difficulty in getting up again. No isolated paresis can be discovered; the patellar reflexes are reduced, especially on the left side. July 8, dead.

The surface of the brain hyperaemic, that of the spinal cord also being rather markedly injected, especially on the posterior surface. The section of the spinal cord greatly swollen, the grey matter looking rather greyish-red. Microscopic examination: Hyperaemia, haemorrhages and considerable oedema, but no cellular infiltration; most of the glia cells are enlarged, clear and transparent; the nerve cells shrunken, homogeneous and deeply stained, highly vacuolated or fenestrated provided with shrunken, diffusely and generally deeply stained nuclei, the surrounding enlarged glia cells having invaded deeply into the nerve cells. In both the medulla oblongata and the spinal cord plenty of white corpuscles are collected in different places in the smaller vessels.



2) *Hilda M.*

The *buccal* specimen, 60 c. c., was, on June 19, injected into *Macacus rhesus* no. 281. July 5, was found lying almost lifeless on the bottom of the cage, died later in the day.

The surface of the brain rather markedly injected and the same applies to the posterior surface of the spinal cord in the cervical region. The section of the spinal cord not swollen but the grey matter has a somewhat reddish tint. Microscopic examination: Rather lively hyperaemia but no haemorrhages and no cellular infiltration, some of the glia cells, especially around the cells of the anterior horns are large, clear, transparent; a great number of the nerve cells being distinctly, though not very highly, changed, shrunken, homogeneous, deeply stained and vacuolated, some of them being invaded by enlarged glia cells, though as a rule not deeply.

3) *John Arvid M.*

The specimen from the *mouth*, 35 c. c., was injected, on June 21, into *Macacus rhesus* no. 284. July 6, seems to be weak, climbs badly and is easy to catch. July 7, the monkey is distinctly weak in the left arm and when jumping, falls on its nose. July 10, the condition unaltered. July 11, dead.

Slight injection of the superficial vessels of both brain and spinal cord. The section of the spinal cord not swollen, the grey matter in the lumbar and dorsal regions rather reddish but not so in the cervical region. In the large bowel an extensive, very marked ulcerative colitis. The mesenteric glands are greatly swollen. Microscopic examination; slight hyperaemia, no haemorrhages and no cellular infiltration; no hypertrophy of the glia cells, a good deal of the ganglion cells have a comparatively normal appearance with distinct tigroid substance, but a few are somewhat homogeneous, slightly shrunken and deeply stained.

5) *Agnes J.*

The *buccal* specimen, 35 c. c., was, on June 20, injected into *Macacus rhesus* no. 282. July 10, climbs badly, the hind legs give way when the animal is running and it is easy to catch, the patellar reflexes are weak. July 12, seems to be still weaker, climbs very badly sometimes falling down. July 15, is exceedingly thin and weak; dies in the evening.

The surface of the brain and cord somewhat injected. On section the spinal cord is not swollen but the grey matter is slightly greyish-

red in the dorsal and lumbar regions. Microscopic examination: Hyperaemia and solitary haemorrhages but no cellular infiltration; some glia cells are rather enlarged; a considerable number of the nerve cells are greatly changed, homogeneous, deeply stained, intensely vacuolated and shrunken, all that remains of those cells of the anterior horns that have undergone the greatest change being only star-shaped or sponge-like masses; the nuclei are generally diffusely and deeply stained, any glia-cell-neuronophagia is hardly noticeable; the changes are most pronounced in the cervical and lumbar enlargements, but also in the medulla oblongata changed nerve cells are to be found.

The monkey which had been inoculated with the specimen from the mouth of the boy John M. presented very slight changes in the spinal cord but developed on the other hand a rather intense ulcerative colitis. This latter must therefore, we suppose, be regarded as the cause of death. The other three monkeys, showed such changes in the spinal cord that the cause of death may be supposed to have been experimental poliomyelitis. In this family, where one case of typical infantile paralysis had occurred, two other members proved to be carriers of the virus of infantile paralysis. If these persons are to be classified as abortive cases or as carriers of the virus, as we have done, is a matter of option. It is, however, remarkable, that they had all suffered from catarrhal symptoms although they had not considered themselves ill. Agnes J. who worked in the same room as the deceased, was also a carrier of the microbe.

\*            \*            \*

*In six families, including the family A., the experimental investigations have thus demonstrated the existence of carriers of the virus. They were always found where*

*their presence could be suspected. In the three families where a greater number of healthy persons were examined, several virus-carriers were found in each family, three in each of the families I. and K. and two in the family M. In each of the families only one typical case with paralysis occurred. One is therefore no doubt justified in assuming that virus-carriers are very common and often in number greatly exceed the clinically positive cases.*

\*       \*       \*

- d) **Investigations made with a view of ascertaining how long the microbe of infantile paralysis remains on the mucous membranes after recovery.**

Our previous investigations have proved the presence of the virus of infantile paralysis on the mucous membranes of the respiratory and digestive tracts in human beings during the acute stage. With the support of the experience gained from other infectious diseases it may, *à priori*, be assumed that a person recovering from infantile paralysis is not free from the organism causing the disease at the time convalescence begins. If such really be the case, an individual who has been restored to health must, as long as he harbours the micro-organism, naturally be able to spread the virus in the same manner as a patient in whom the disease is still active. *It must therefore be of great importance from a practical, prophylactic point of view to ascertain how long after recovery from the disease the microbe of infantile paralysis persists on the mucous membranes of convalescent cases.* Attention has also recently been drawn to the fact that persons who have recovered from the disease possibly play the rôle

of propagators of the infection. OSGOOD and LUCAS have tried to solve the problem by determining the length of time the virus may be demonstrated in the nasal mucous membrane of monkeys which have recovered from an infection caused by an intracerebral injection. They found it still present after a period of six months.

As the presence of the virus could without too great difficulties be demonstrated in the secretions from persons affected by infantile paralysis in the acute stage, we have tried to determine also how long after the acute stage of the illness was over the virus could be detected. With this object those persons who had previously been the subjects of our investigation, and in whom we had succeeded in demonstrating the presence of the virus, have, at different intervals, been subjected to repeated washings of the nose, mouth, pharynx and intestine. The specimens thus obtained have, in the same way as before, been filtered and then injected intraperitoneally and into one sciatic nerve of monkeys. As stated above, three of the patients on whom investigations were made succumbed to the disease. The number of those on whom after-investigations could be performed has thus been reduced to nine.

The accounts of the disease of the patients in question are found on pp. 53—81.

*Case XVI. Ingrid S.*

On Sept. 30, 1911, the first washing of the mouth and intestine was performed.

The specimen from the *mouth* was, on Oct. 1, injected into *Macacus cynomolgus* no. 52. The monkey died on Oct. 8. The spinal cord showed considerable cellular infiltration in the grey matter and intense leucocyte-neuronophagia of the cells of the anterior horns. Three control animals inoculated with the spinal cord died of experimental poliomyelitis.



The *intestinal* specimen was injected simultaneously with that from the mouth into *Macacus cynomolgus* no. 53. On Oct. 8, the animal developed paresis of both arms and, on Oct. 14, complete paralysis of both legs, dying the following day. The spinal cord showed intense cellular infiltration in groups and around the vessels. Leucocyte-neuronophagia and complete destruction of the ganglion cells.

On Oct. 20, *twenty-three days* after the onset of the disease a second washing of the mouth, pharynx and intestine was performed.

Of the specimen from the *mouth* 90 c. c. were, on Oct. 21, injected intraperitoneally into *Macacus cynomolgus* no. 95. Oct. 23, climbs and runs slowly and seems weak in the hind legs. Oct. 25, runs with a limp and when jumping the legs give way. Oct. 26, the right arm is held in the position of radial paresis, tumbles on the nose. Oct. 27, is sitting shaking in the whole body, is paretic in both arms, walks exceedingly slowly, tumbling on the nose. Oct. 28, dead.

The vessels on the surface of the brain are moderately injected but the surface of the spinal cord is rather pale. The section of the spinal cord is swollen in the lumbar region, the grey matter is distinctly marked and everywhere greyish-red discoloured. The microscopic examination shows hyperaemia and haemorrhages, accumulation of white corpuscles in the vessels and sometimes perhaps a slight cellular infiltration around the same; hypertrophy of the glia cells and intense degeneration of the majority of the nerve cells, of which some are very pale, almost dissolved, others again homogeneous, vacuolated and markedly reduced, the surrounding enlarged glia cells having invaded deeply into them. Karyolysis of the nuclei.

The specimen from the *intestine*. On Oct. 21, 100 c. c. were injected intraperitoneally into *Macacus cynomolgus* no. 94. Nov. 6, climbs rather slowly and does not run quite naturally, on jumping the hind legs give way. Dec. 10, found dead.

Marked injection of the soft membranes of the brain and a distinct contrast between cortex and medulla. The membranes of the spinal cord are also injected on the posterior surface, the section of the spinal cord is swollen, the grey matter is distinctly marked and of a vivid reddish colour. The microscopic examination shows marked hyperaemia and oedema, but neither haemorrhages nor cellular infiltration; the glia cells are hypertrophied and the nerve

cells degenerated and invaded by the glia cells in a manner similar to that found in the spinal cord of the preceding monkey.

On Oct. 31, *the 34th day* after the onset of the disease, a third washing of the mouth and intestine of the girl was performed.

The specimen from the *mouth*. On Nov. 3, 120 c. c. were injected intraperitoneally into *Macacus rhesus* no. 127. Nov. 19, climbs slowly and with jerks. Nov. 21, the same observation. Dec. 5, runs and climbs slowly, is swollen in the face. Dec. 6, has still oedema of the face, can hardly be induced to run, tumbles every now and then on the nose, the knees of the hind legs giving way. Dec. 19, squatting in the cage, if taken out and induced to walk it falls and finds great difficulty in rising, seems weak in all the extremities, the oedema of the face has increased. Dec. 20, dead.

The superficial vessels of the brain and of the posterior aspect of the spinal cord are somewhat injected, the cerebral cortex is rather rich in blood. The section of the spinal cord is slightly swollen and the grey matter everywhere of a greyish-red colour. Microscopic examination: Slight hyperaemia with scattered haemorrhages, no cellular infiltration, marked hypertrophy of the glia cells and considerable degeneration of the majority of the nerve cells, which are deeply stained, shrunken and greatly encroached upon by hypertrophic glia cells, often nothing but small, irregular lumps of protoplasm remaining of the nerve cells; karyolysis of the nuclei.

Of the specimen from the *intestine* 100 c. c. were injected, on Nov. 3, into the peritoneum of *Macacus rhesus* no. 123. Nov. 23, climbs remarkably slowly and with great difficulty, when running the hind legs give way, after a short while the animal is perfectly exhausted and does not want to walk at all. In the evening it lies almost motionless and dies later on in the night.

The soft membranes of the brain and the spinal cord are rather vividly injected, the contrast between the cortex and the medulla is sharp. On section the spinal cord is moist, not swollen, the grey matter is sharply marked and distinctly reddish with distinct fine red spots. Microscopic examination: Hyperaemia and numerous haemorrhages, no cellular infiltration but sometimes a distinct accumulation of the white corpuscles in the vessels; no hypertrophy of the glia cells, the majority of the nerve cells are not perceptibly

changed, though a small number of them are homogeneous, deeply stained and shrunken; karyolysis of the nuclei.

The last washing of the mucuous membranes in question was performed on April 17, 1912, 203 days after the onset of the disease. One of the monkeys inoculated with the specimens died of bacterial peritonitis. The other one showed no signs of disease after the injection.

The experiments have proved that the specimens taken on the 23rd and 34th day after the onset of the disease still contained the virus of infantile paralysis and this in a sufficiently virulent condition to cause, after injection, experimental poliomyelitis with more or less distinct pareses and fatal termination. The specimen from the intestine obtained on the 203rd day, on the other hand, gave rise to no symptoms in the animal injected.

#### *Case XVII. Sigrid Maria R.*

On Oct. 3, the first washing of the mouth and intestine was performed.

The specimen from the *mouth* was injected, on Oct. 15, into *Cynocephalus hamadryas* no. 61. The animal remained well.

Of the specimen from the *intestine* 130 c. c. were injected intraperitoneally, on Oct. 3, into *Cynocephalus hamadryas* no. 57. The following day the Baboon climbed and ran less lively than ordinarily. On Oct. 5 it was probably somewhat weak in the left hand and was easy to catch. After that it climbed slowly and with some difficulty for some time but ultimately recovered.

On Oct. 20, 35 days after the onset of the disease, a second washing of the girl's mouth and pharynx was performed. The injection of the specimen caused no change with regard to the health of the monkey inoculated.

On Nov. 9, the third washing of the mouth and

intestine was performed, *45 days* after the onset of the disease.

The specimen from the *mouth*, 120 c. c., was, on Nov. 15, injected into *Macacus rhesus* no. 149. Nov. 19, the monkey is thin and weak, climbs and runs badly, limps in the hind legs. Nov. 20, climbs still worse, does not want to run. Nov. 23, still weaker and can climb only with the greatest difficulty, tumbles over when jumping, the knees of the hind legs giving way. Nov. 24, paresis of the left hand, in the evening paresis also of the left arm. Nov. 26, dead.

The pia of the brain, especially at the base, vividly hyperaemic and that of the spinal cord also slightly injected. The section of the spinal cord swollen in the cervical region, the grey matter being here and, though less markedly, also in the dorsal and lumbar regions somewhat greyish-red. Microscopic examination: Slight hyperaemia, haemorrhages and, in the cervical region, oedema, no cellular infiltration; hypertrophy of the glia cells and considerable changes of the nerve cells which are deeply stained, homogeneous, vacuolated and, owing to an invasion of hypertrophic glia cells, reduced to small, irregular masses.

A filtrate of the emulsion of the spinal cord was, on Dec. 30, inoculated into the peritoneum and one sciatic nerve of *Cercopithecus fuliginosus* no. 218. It died on Febr. 21 after having been perceptibly weak for some time, but without exhibiting any isolated paralysis.

The surface of the brain vividly injected, the contrast between the cortex and the medulla sharp. The section of the spinal cord is not swollen, the grey matter is of a marked greyish-red colour with fine red dots and streaks. Microscopic examination: Intense hyperaemia and numerous haemorrhages; distinct hypertrophy of the glia cells especially around the vessels and the cells of the anterior horns; the nerve cells are on the whole only slightly changed but a few of them are shrunken and deeply stained with a diffusely and generally deeply stained nucleus, into a few of the nerve cells enlarged glia cells have eaten their way.

The *intestinal* specimen, 140 c.c., was, on Nov. 15, injected into *Macacus rhesus* No. 147 without in any way influencing the good health of the animal.

On April 16, the *204th day* after the onset of the disease, a fourth washing of the mouth and intestine was performed.



The specimen from the *mouth*, 90 c. c., was, on April 20, injected into *Macacus rhesus* no. 264. On June 8 the animal was sitting on the bottom of the cage and did not want either to walk nor to climb. It died later in the day.

The membranes as well as the substance of the brain markedly hyperaemic, the surface of the spinal cord being likewise injected. The section of the spinal cord scarcely swollen, the grey matter somewhat reddish, especially in the cervical region. Microscopic examination: Hyperaemia and, in the cervical cord, rather large haemorrhages and oedema, distinct hypertrophy of some of the glia cells; a great number of the nerve cells, especially in the cervical cord, are much changed, shrunken, deeply stained, homogeneous and intensely vacuolated, some of them being deeply invaded by the surrounding glia cells; of some of the nerve cells there remain nothing but star-like or sponge-like masses; the nuclei are diffusely and generally deeply stained.

The *intestinal* specimen, 80 c. c., was, on April 20, injected into *Macacus rhesus* no. 265 but the health of the animal suffered in no perceptible way therefrom.

The investigation of the specimens have thus shown that the *buccal secretion contained virulent microbes of infantile paralysis still more than six months after the onset of the disease*, whereas we only at the first washing probably succeeded in demonstrating their presence in the intestinal secretion.

*Case XIX, Erik Wilh. N—g.*

On Oct. 8 the mouth, pharynx and intestine of the boy were washed.

Of the specimen from the *mouth*, 60 c. c. were injected, on Oct. 11, into *Macacus rhesus* no. 74. The animal remained well.

Of the *intestinal* specimen 125 c. c. were injected, on Oct. 12, into *Macacus cynomolgus* no. 75. Complete paralysis of both legs developed on Oct. 23 and the animal died on Oct. 26. The spinal cord showed perivascular cellular infiltration, far advanced leucocyte-

neuronophagia and complete destruction of the cells of the anterior horns.

On Oct. 21, *21 days* after the onset of the disease, another washing of the boy's mouth and intestine was performed.

The specimen from the *mouth*, 120 c. c., was injected, on Oct. 26, into *Macacus rhesus* no. 107. Oct. 28, the monkey climbs slower than usually. Oct. 31, is easy to catch and on jumping the legs give way. Nov. 1, looks ill, does not readily grasp with the left hand; respiration laboured. Nov. 2, runs and climbs, but not very quickly, prefers sitting still, has no distinct pareses. Nov. 6, is sitting still, panting, does not want to run, climbs with great difficulty, if pushed over, the animal finds difficulty in getting up. Nov. 7, the condition about the same. Nov. 9, sits stooping, has possibly some paresis of the left hind leg and slight paresis of the left hand which is usually held raised. Nov. 10, dead.

Vivid hyperaemia on the surface of both brain and spinal cord, the cortex being greyish-red. The section of the spinal cord everywhere swollen, moist and the grey matter of a deep reddish colour. A caseous pneumonia in the inferior lobe of the right lung, caseating bronchial glands and miliary tubercles in the liver, spleen and peritoneum. The microscopic examination shows marked hyperaemia, haemorrhages and oedema in the spinal cord but no cellular infiltration; some of the glia cells are hypertrophied and the majority of the nerve cells in the entire spinal cord are shrunken, deeply stained, intensely vacuolated and invaded by surrounding, enlarged, glia cells, only small star-shaped bodies often being all that is left of the nerve cells.

The specimen from the *intestine*. On Oct. 31 100 c. c. were injected into *Macacus rhesus* no. 113 without causing any visible change with regard to the health of the animal.

The third washing of the mouth and intestine was performed on Nov. 20, the *52nd day* after the onset of the disease.

The specimen from the *mouth*. On Nov. 21 80 c. c. were injected into *Macacus rhesus* no. 162. Dec. 12, it climbs slowly and with difficulty. Dec. 12, is sitting huddled up, walks remarkably slowly, swaying the body, if pushed over, it finds great difficulty in getting

up again, cannot be made to climb but is able to hold on by the hands. Dec. 13, dead.

The pia of the brain and the cortex are rather hyperaemic. The superficial vessels of the spinal cord are not distended with blood, the section of the spinal cord is moist but scarcely swollen, the grey matter is faintly greyish-red, especially in the lumbar region. A small, recent pneumonia in the posterior and lower part of the inferior lobe of the right lung and a still smaller one in the middle lobe. Microscopic examination: Rather marked hyperaemia and haemorrhages, especially in the medulla oblongata, accumulation of the white corpuscles in the vessels in different places; possibly a slight cellular infiltration around them; the glia cells are hypertrophied and a great number of the nerve cells are considerably changed, some of them being pale, transparent, others again deeply stained, homogeneous and more or less intensely encroached upon by the surrounding, enlarged glia cells.

On Dec. 30 *Cercopithecus fuliginosus* no. 216 was inoculated into one sciatic nerve with an emulsion of the spinal cord of the preceding monkey. The animal died on Febr. 17, nothing remarkable having previously been observed.

The superficial vessels of the brain are vividly injected, there is a sharp contrast between the cortex and medulla. The section of the spinal cord slightly swollen and the grey matter of a light greyish-red colour. Microscopic examination: Moderate hyperaemia, only few haemorrhages and no cellular infiltration, distinct hypertrophy of the glia cells and degeneration of the nerve cells of which some are homogeneous, deeply stained and shrunken and sometimes invaded by the large, clear, surrounding glia cells, a few being very pale, finely granular, as if dissolved.

The specimen from the *intestine*. On Nov. 21, 75 c. c. were injected into *Macacus rhesus* no. 163. The animal remained apparently in good health for more than three months. On March 18 it was observed to climb with difficulty, being weak in the hind legs. March 19, dead.

The surface of the brain markedly hyperaemic in its anterior parts and at the base of the brain, the contrast between the cerebral cortex and the medulla being distinct. The surface of the spinal cord is slightly injected. The grey matter is, especially in the cervical and dorsal regions, of a distinct greyish-red colour. Microscopic examination: Hyperaemia and marked perivascular cellular infiltra-

tion in the medulla oblongata, slight hyperaemia and solitary haemorrhages in the grey matter of the spinal cord, hypertrophy of the glia cells and marked degeneration of the nerve cells which are encroached upon by the surrounding, enlarged glia cells to such a degree that there remain only small, irregular, darkly coloured lumps; the changes of the nerve cells are most pronounced in the lumbar and dorsal regions.

On March 8, *158 days* after the onset of the disease, we collected for the fourth time specimens of the secretions from the mucuous membranes of the mouth and intestine.

The specimen from the *mouth* was, on March 12, injected into *Cercopithecus fuliginosus* no. 234, which received 130 c. c. The animal was found dead on March 20, nothing remarkable having previously been observed.

The superficial vessels of both brain and spinal cord were rather vividly injected. The section of the spinal cord swollen in the dorsal region and the grey matter everywhere somewhat greyish-red. Microscopic examination: No distinct hyperaemia, no haemorrhages and no cellular infiltration, but a marked hypertrophy of the neuroglia cells and degeneration, though not very far advanced, of the nerve cells of which some are pale, homogeneous, transparent, others shrunken, deeply stained and vacuolated and often more or less encroached upon by the surrounding glia cells.

The *intestinal* specimen, 80 c. c., was, on March 11, injected into *Macacus rhesus* no. 239. The animal died suddenly on March 19.

The surface as well as the cortex of the brain markedly injected. The surface of the spinal cord slightly injected, the grey matter in the lumbar and dorsal regions having a pale greyish-red colour. Microscopic examination: Considerable hyperaemia and numerous haemorrhages, no cellular infiltration, but in some of the smaller vessels of the cervical cord there is a distinct accumulation of white blood corpuscles; the glia cells are hypertrophied and the nerve cells degenerated, even if not highly so, shrunken, homogeneous, deeply stained and sometimes more or less deeply invaded by enlarged glia cells.

The boy has harboured the microbe of infantile paralysis in a virulent state on his mucuous membranes during the whole time he was a subject of investigation.



And this has, nevertheless, been extended over more than five months. With regard to the monkey which was inoculated with the intestinal specimen taken on the 52nd day and died four months after the injection, the question might naturally arise whether it had not been infected by some other monkey. We shall come back to this point later on. As regard the correctness of our conclusion as to the presence of the microbe in the boy such a possibility is of no importance, in as much as the presence of the virus was also demonstrated in the specimen obtained at the last intestinal irrigation.

*Case XX. Elsa N—g.*

On Oct. 12 the mouth and intestine of the girl were washed.

The specimen from the *mouth* was, on Oct. 16, injected into *Macacus cynomolgus* no. 78. The animal was found dead on Dec. 26; no symptoms of disease had previously been observed. The spinal cord showed haemorrhages, but no cellular infiltration, considerable degeneration of the majority of the nerve cells in the entire spinal cord, these being greatly shrunken and vacuolated, homogeneous and deeply stained.

The *intestinal* specimen was injected into *Macacus cynomolgus* no. 77, on Oct. 13; it died paralyzed on Oct. 17. The microscopic examination of the spinal cord showed hyperaemia, haemorrhages, oedema, commencing neuronophagia and karyolysis of the nerve cells.

On Oct. 20, *the 12th day* after the onset of the disease, the girl was subjected to another washing of the mouth and intestine.

The specimen from the *mouth*, 125 c. c., was injected, on Oct. 24, into *Macacus rhesus* no. 98. Oct. 26, looks thin and ill, climbs and runs slowly and is easy to catch. Nov. 28, dead.

Moderate hyperaemia of the pia of the brain, most pronounced at the base, around the pons and medulla oblongata. The vessels on the surface of the spinal cord are everywhere greatly

distended, on section the spinal cord moderately swollen, moist, the grey matter showing a greyish-red discolouration. Microscopic examination: Hyperaemia in the medulla oblongata, less marked in the spinal cord, no haemorrhages and no cellular infiltration; the glia cells are large, clear, transparent and the nerve cells generally more or less degenerated, some have an apparently normal nucleus, but a pale and rather homogeneous cell body, while the majority are shrunken, homogeneous, deeply stained, with greatly changed nuclei and trimmed by large, clear glia cells which often have penetrated more or less deeply into the nerve cells.

Of the specimen from the *intestine* 100 c. c. were injected, on Oct. 24, into *Macacus rhesus* no. 101, into the peritoneum and into both sciatic nerves. Dec. 2, climbs very badly, falls on its nose when trying to jump, is weak in the arms and also in the left leg. Dec. 5 distinct paresis of both arms, tumbles repeatedly on the nose, when trying to walk. Dec. 6, cannot climb, the paresis of the right arm increased; otherwise same as yesterday. Dec. 7, sitting in a stooping position not wanting to move, the hands plainly in radial paralysis-position. Dec. 8, dead.

The brain without any macroscopical change and the surface of the spinal cord not hyperaemic. The section of the spinal cord not swollen, but the grey matter everywhere distinctly reddish and spotted with red. In the lower lobe of the right lung a small, recent pneumonia. Microscopic examination: Hyperaemia, no haemorrhages and no cellular infiltration, hypertrophy of some of the glia cells; the greater part of the nerve cells being degenerated, vacuolated, provided with dark, diffusely stained nuclei, some pale, extremely finely granular, as if in a state of dissolution, others shrunken, homogeneous and deeply stained and sometimes encroached upon by the surrounding, large, clear cells.

On Febr. 1, *116 days* after the onset of the disease, a third washing of the mouth and intestine was performed on the girl.

The specimen from the *mouth*, 100 c. c., was injected on, Febr. 2, into *Macacus rhesus* no. 245. Febr. 3, is looking ill and does not want to run. Febr. 7, dead. The post-mortem examination revealed a sero-fibrinous peritonitis and a slight double-sided fibrinous pleurisy. The spinal cord showed no change worth mentioning. On cultivation some colonies of cocci were obtained.

Of the *intestinal* specimen 120 c. c. were injected, on Febr. 2, into *Macacus cynomolgus* no. 244. Febr. 9, in the morning, climbs slowly and is weak, died in the evening.

The vessels on the surface of the brain vividly injected and the contrast between the cortex and medulla unusually well marked. The surface of the spinal cord is pale, the section slightly swollen and the grey matter faintly reddish. Microscopic examination: Hyperaemia and sometimes rather large haemorrhages but no cellular infiltration; hypertrophy of some of the glia cells; a smaller portion of the nerve cells have a comparatively normal aspect, but the majority are more or less changed, shrunken, deeply stained, homogeneous and often deeply invaded by surrounding, enlarged glia cells.

The monkey inoculated with the specimen obtained at the last washing of the mouth died of secondary infection, and it is thus impossible to decide, whether the buccal secretion still contained the microbe. That the intestinal specimen harboured the microbe there is no doubt about, as the injection of same caused intense and wide-spread changes in the spinal cord of the animal.

#### *Case XXIII. Harry R—m.*

On Oct. 12 the boy was subjected to the first washing of the mouth and intestine.

The specimen from the *mouth* was, on Oct. 17, injected into *Macacus cynomolgus* no 82. The animal was found dead five days later, nothing remarkable having been observed on the previous day. The spinal cord showed hyperaemia, haemorrhages, degeneration of the nerve cells and glia-cell-neuronophagia but no cellular infiltration.

The *Macacus cynomolgus* which had been injected with the specimen from the *intestine* died the following day. The peritoneal cavity contained an inconsiderable quantity of a rather clear fluid with a few bacteria.

On Oct. 21, 12 days after the onset of the disease, a second washing of the mouth and intestine was performed.

Of the specimen from the *mouth* 120 c. c. were, on Oct. 27, injected into *Macacus rhesus* no. 108. Nov. 1, does not climb as quickly as before. Nov. 6, is easy to catch, runs with the back curved. Nov. 7, looks ill but has no distinct paresis, diarrhoea. Nov. 8, distinct paresis of both front legs, especially of the left, is apt to fall on the nose when running. Nov. 9, same as yesterday, falls on the nose but is able to hang on by the hands, paresis of the muscles of the shoulder-joints. Nov. 10, moves slowly, joggingly, does not topple over as easily as before but is easily made to fall. Nov. 11, walks very carefully keeping the body motionless, bent. Nov. 12, is most paretic in the right arm. Nov. 13, dead.

The superficial vessels of the brain are moderately distended with blood and the cerebral cortex has a slight reddish tint. The pia corresponding to the enlargements of the cord is hyperaemic, the section of the spinal cord rather swollen, moist and the grey matter everywhere distinctly greyish-red. In the lower lobe of the left lung a caseating focus of the size of a pea and a resent pneumonia posteriorly. Microscopic examination: Hyperaemia, sometimes rather large haemorrhages but no cellular infiltration, hypertrophy of some of the glia cells and degeneration of the nerve cells, which are shrunken, deeply stained and vacuolated with pyknotic nuclei and sometimes also invaded by enlarged glia cells.

The *intestinal* specimen, 120 c. c., was, on Oct. 21, injected into *Macacus rhesus* no. 105. The animal seemed apparently well for several months but died suddenly on March 19.

The vessels on the surface of the brain intensely injected, the cortex being also hyperaemic. Rather marked injection visible also over the spinal cord, the grey matter being distinctly reddish. A caseating focus of the size of a pea in one of the lungs and a similar one in one of the bronchial glands. Microscopic examination: Rather considerable hyperaemia, haemorrhages and hypertrophy of the glia cells; the majority of the nerve cells are degenerated and the surrounding, large, clear glia cells have invaded them, sometimes rather deeply, especially in the lumbar enlargement, but also in the dorsal region.

A third washing of the *intestine* was performed on the boy on Nov. 25, *the 47th day* after the onset of the disease.



The specimen obtained, 100 c. c., was injected into *Macacus rhesus* no. 176, on Dec. 1. The monkey died suddenly on Febr. 26, nothing remarkably having been observed on the day previous.

The surface of the brain vividly injected, that of the spinal cord less. The section of the spinal cord not swollen, the grey matter only slightly reddish. Microscopic examination: Rather considerable hyperaemia in the grey matter, and haemorrhages, more especially in the cervical region, no cellular infiltration; hypertrophy of the glia cells; degeneration of the majority of the nerve cells, of which some are pale, transparent, very finely granular, others, again, deeply stained, homogeneous, shrunken, the surrounding, hypertrophied glia cells having eaten their way into a great number of them.

On Febr 5, *119 days* after the onset of the disease, a fourth washing of the mouth and intestine of the boy was performed.

Of the specimen from the *mouth* 80 c. c. were, on Febr. 8, injected into *Macacus pileatus* no. 250. The monkey died on Febr. 21, without having shown any pareses.

The surface of the brain is markedly hyperaemic and that of the spinal cord shows also a moderate degree of injection of the vessels. The section of the spinal cord much swollen, the grey matter being in the lumbar enlargement of a pale greyish-red colour. Microscopic examination: Slight hyperaemia, marked oedema but no haemorrhages; distinct hypertrophy of the glia cells only around the neurons; degeneration of the nerve cells which are deeply stained, homogeneous, shrunken and often markedly encroached upon by the hypertrophied cells of the surrounding glia.

Of the *intestinal* specimen 80 c. c. were injected, on Febr. 9, into *Macacus pileatus* no. 251. Febr. 28, looks thin, climbs slowly. March 4, is exceedingly ill; is killed.

The surface of the brain rather vividly injected, that of the spinal cord pale. On section the spinal cord is not swollen and the grey matter is not red. On microscopic examination no distinct changes are to be observed in the cord.

The monkey inoculated with the last intestinal specimen showed neither clinical symptoms nor anatomical changes which justify the presumption

of poliomyelitis. But otherwise the specimens have contained the microbe of infantile paralysis every time the boy has been examined during the four months nearest following the onset of the disease.

*Case XXIV. Astrid L—n.*

On Oct. 15 a washing of the mouth and intestine of the patient was performed.

*Macacus cynomolgus* no. 86 was, on Oct. 19, injected with 120 c. c. of the *buccal* specimen, but remained, as far as could be ascertained, well during three months of observation.

*Macacus cynomolgus* no. 86 was injected, on Oct. 18, with 60 c. c. of the *intestinal* specimen. It died paralyzed on Oct. 27. The spinal cord showed possibly a slight cellular infiltration around the vessels; considerable degeneration of the cells of the anterior horns and neuronophagias due to glia cells.

On Oct. 26, the 12th day after the onset of the disease, another washing of the mouth and intestine was performed on the girl.

Of the specimen from the *mouth* 100 c. c. were, on Nov. 2, injected into *Macacus rhesus* no. 122. Nov. 8, climbs rather slowly and with jerks. Nov. 9, markedly paretic in the left foot, which sometimes becomes twisted, the animal running on the dorsal surface. Nov. 10, still marked paresis of the left foot, slips on it now and then, when climbing. The condition unaltered on the whole until Nov. 19, when the animal was observed to be climbing very slowly. Nov. 20, found dead.

The surface of the brain rather markedly hyperaemic and the cortex greyish-red. The vessels on the posterior surface of the spinal cord moderately injected, the section of the spinal cord not swollen, the grey matter distinctly marked and, at least in the lumbar cord, somewhat reddish. Microscopic examination: Rather considerable hyperaemia, scattered haemorrhages, especially in medulla oblongata, some oedema, but no cellular infiltration; marked hypertrophy of some of the glia cells; the majority of the nerve cells show karyolysis, destruction of the tigroid substance and deep staining of the cell body, some of the cells, especially in the lumbar

enlargement, being shrunken, vacuolated and trimmed with and encroached upon by enlarged, clear glia cells.

The *intestinal* specimen, 140 c. c., was, on Nov. 2, injected into *Macacus rhesus* no. 121. Nov. 7, it climbs somewhat more slowly than before. Nov. 11, the animal is unsteady in its movements and slips when jumping. Nov. 12, is lying almost motionless on the bottom of the cage, breathing slowly and irregularly. Nov. 13, dead.

The surface of the brain and spinal cord posteriorly and over the enlargements vividly injected. On section the spinal cord swollen and the grey matter, especially in the dorsal region, reddish discoloured. Microscopic examination: Hyperaemia, especially in the lumbar region, haemorrhages, perhaps in solitary places a slight infiltration round the vessels; hypertrophy of the glia cells; considerable changes of the nerve cells, some of which are pale, bluish, almost dissolved, others deeply stained, shrunken, homogeneous and trimmed by enlarged glia cells which sometimes have eaten their way far into the nerve cells.

The third washing of the mouth and intestine of the girl was performed on Nov. 10, 29 days after the onset of the disease.

The specimen from *the mouth*, 115 c. c., was, on Nov. 18, injected into *Macacus rhesus* no. 157. Nov. 21, climbs badly and slowly and runs slowly too, dragging the tips of the feet, especially of the left one, along the floor. Nov. 22, breathes heavily. Nov. 23, dead.

Marked hyperaemia of the surface of the brain as well as of the spinal cord, the cerebral cortex being greyishly-red discoloured. On section the spinal cord does not swell but is moist and the grey matter, especially in the cervical cord, is distinctly reddish. A recent pneumonia in the left lung and in the lower lobe of the right lung. Microscopic examination: Hyperaemia, haemorrhages, slight hypertrophy of the glia cells, the nerve cells showing, as a rule, a distinct tigroid substance and apparently rather normal nuclei, some of them being, however, somewhat shrunken, slightly homogeneous and to a slight degree notched by the surrounding glia cells.

Of the *intestinal* specimen 100 c. c. were, on Nov. 17, injected into *Macacus rhesus* no. 158. Nov. 19, climbs rather slowly and with jerks. Nov. 24, the condition about the same as previously

excepting that the fore legs give way on jumping. Nov. 25, climbs slowly, no distinct, isolated paralysis. Nov. 26, dead.

The pia of the brain and spinal cord vividly injected. On section the spinal cord swollen, the grey matter sharply marked and plainly reddish, especially in the lumbar enlargement. Microscopic examination: considerable hyperaemia, haemorrhages in the lumbar enlargements, some hyperleucocytosis in the small vessels, the glia cells are hypertrophied and the nerve cells degenerated with a nucleus that is either diffusely or not at all stained and without any tigroid substance, homogeneous, deeply stained and often encroached upon by surrounding, large, clear glia cells.

On Febr. 9, *the 120th day* after the onset of the disease, the last washing of the mouth and intestine was performed on the girl.

The specimen from the *mouth* was first filtered through a Heim and then through a Berkefeld filter. To the filtrate was added an equal quantity of sterilised bouillon and the mixture placed in a thermostate until March 6. On microscopical examination the fluid was then found to contain a long, thick rod on account of which it was once more filtered through a Heim filter. Now 2 c. c. were injected into one sciatic nerve of *Macacus pileatus* no. 227. March 10, in the morning, the monkey is lying on the bottom of the cage perfectly stiff in the hind legs and with intense spastic contractions of the body, the head being turned a little. At noon it looks better and runs fairly well, the legs, especially the left one, being, however, tossed about, climbs slowly, when held up the hind legs are observed to shake a little. March 11, the animal remains mostly lying on the bottom of the cage, when walking or running the movements are ataxic and reeling, does not feel flaccid, on the contrary the body being rather stiff; patellar reflexes are present on both sides though somewhat weak. March 12, the gait is still highly ataxic. March 13, dead.

The surface of the brain rather vividly injected and the superficial vessels of the spinal cord are likewise rather much distended with blood. The grey matter of the spinal cord is greyish-red in the lumbar region, but otherwise not. A culture from the spinal cord gave no bacteria. The microscopic examination showed hyperaemia and numerous, rather large haemorrhages; a moderate



degree of enlargement of the glia cells; the ganglion cells being somewhat shrunken, deeply stained and highly vacuolated; only a few glia-cell-neuronophagias.

The *intestinal* specimen was treated in the same manner as the specimen from the mouth. March 4, a kind of cocci have grown. After filtration through a Heim 1, 5 c. c. were injected into one sciatic nerve of *Macacus cynomolgus* no. 226. The animal remained well.

The secretional specimens from the girl taken a fortnight after the onset of her illness have undoubtedly contained virulent microbes of infantile paralysis. Also the intestinal fluid from the 29th day has caused such changes in the spinal cord of the monkey inoculated therewith, that it seems justifiable to consider them as due to poliomyelitis, the more so as the small, recent pneumonia cannot explain them satisfactorily. With regard to the monkey inoculated with the buccal specimen of the same day it can hardly be considered that it has been suffering from poliomyelitis as the spinal cord only presented slight change but, on the other hand, a large pneumonia was found, sufficient to explain the fatal result. Nor did the intestinal specimen taken 120 days after the onset of the disease cause any changes in the animal inoculated. On the other hand the monkey injected with the specimen from the mouth showed symptoms that remind of poliomyelitis. Still the changes observed in the spinal cord were, excepting the haemorrhages, not very considerable.

#### *Case XXV. Erik S—m.*

The first washing of the mouth and intestine was performed on Oct. 15.

*Macaci cynomolgi* nos. 83 and 84 were, on Oct. 18 injected with the specimen from the *mouth*. The former became paralyzed on Oct. 28 and died the following day. The spinal cord showed hyperaemia and haemorrhages, but no distinct cellular infiltration, hypertrophy of the glia-cell and degeneration of the ganglion cells, as

well as glia-cell-neuronophagia. The other monkey, no. 84, became paralyzed in both arms, on Oct. 25, and died on Oct. 28. The microscopic examination presented hyperaemia and solitary haemorrhages but scarcely any quite definite cellular infiltration; enlargement of the majority of the glia cells, degeneration of the nerve cells and glia-cell-neuronophagias.

Two *Macaci cynomolgi* were likewise injected with the *intestinal* specimen, no. 80 receiving 80 c. c. and no. 81 30 c. c. The former exhibited general debility and died on Oct. 20. The spinal cord showed slight hyperaemia, no distinct cellular infiltration, slight degeneration of the nerve cells but no neuronophagias. With regard to the latter monkey nothing was observed until Dec. 9, when it climbed badly, ran slowly and tumbled on its nose. It died the following day. The microscopic examination showed hyperaemia, haemorrhages, enlargement of the glia cells and considerable degeneration of the nerve cells.

On Oct. 26, the *13th day* after the onset of the disease, the boy was subjected to another washing of the mouth and intestine.

Of the specimen from the *mouth* 110 c. c. were injected, on Oct. 31, into *Macacus rhesus* no. 114. Nov. 1, runs and climbs rather more carefully than previously. Nov. 2, is easy to catch, climbs remarkably slowly and carefully, with some difficulty and with jerks. Nov. 6, dead.

The surface of the brain rather vividly injected at the base, but the spinal cord is pale, on transverse section the cord not swollen and the grey matter is indistinct. A large pneumonia in the lower lobe of the left lung, large pneumonias and caseating foci in the right lower lobe, caseating bronchial glands and tubercles in the liver and the spleen. Microscopic examination: Slight hyperaemia, haemorrhages, chiefly in the cervical cord, only a few glia cells show signs of hypertrophy; the nerve cells generally of normal appearance with distinct tigroid substance; solitary ganglion cells being somewhat homogeneous and deeply stained, showing signs of commencing karyolysis.

On Nov. 6, *Macacus rhesus* no. 132 was inoculated into one sciatic nerve with an emulsion of the spinal cord. Dec. 31, the monkey is thin, runs slowly, does not like to climb and is weak in the hind legs. Jan. 2, dead, Microscopic examination showed

hyperaemia, no haemorrhages and no cellular infiltration but some oedema, hypertrophy of the glia cells, degeneration of the nerve cells and neuronophagias.

100 c. c. of the *intestinal* specimen were injected, on Nov. 1, into *Macacus rhesus* no. 116, no disturbances with regard to the health of the animal being noticed.

The third washing of the mouth and intestine of the little boy was performed on Nov. 12, 30 days after the onset of the disease.

105 c. c. of the specimen from the *mouth* were, on Nov. 17, injected into *Macacus rhesus* no. 155. Nov. 19, the animal is somewhat less lively and climbs slowly. The same condition prevailed until Dec. 22, when it looks ill, remains on the floor of the cage, climbs and runs badly and seems to be weak in both hind legs. In the evening the monkey is lying on the floor of the cage, vainly striving to get up by the aid of the arms, the legs being completely paralyzed. Dec. 23, dead.

The pia of the brain as well as of the spinal cord hyperaemic. The grey matter of the spinal cord of a distinct reddish discoloration, especially in the lumbar enlargement. Microscopic examination: Marked hyperaemia and haemorrhages but no cellular infiltration; hypertrophy of the glia cells; the majority of the nerve cells in the whole spinal cord are deeply stained, homogeneous, shrunken, the tigroid substance dissolved and the nucleus diffusely and deeply stained, besides which they are greatly encroached upon by the surrounding, hypertrophied glia cells.

The *intestinal* specimen, 100 c. c., was, on Nov. 17, injected into *Macacus rhesus* no. 154 without giving rise to any signs of disease.

Still another washing of the mouth and intestine of the boy was performed on April 20, 190 days after the onset of the disease.

120 c. c. of the specimen from the *mouth* were injected, on April 23, into *Macacus rhesus* no. 267 without causing any apparent change with regard to the health of the animal.

The *intestinal* specimen was injected the same day into *Macacus rhesus* no. 268. The animal died three days later of peritonitis.

The specimen of intestinal secretion, obtained from the boy on the 13th day after the onset of the disease caused no illness in the inoculated animal. The monkey injected with the buccal fluid died, it is true, but as extensive pneumonias and also tuberculosis were found present, and the histological changes in the spinal cord were comparatively insignificant, it was all the same rather uncertain, whether the secretion had contained any virulent microbes of infantile paralysis. In order to ascertain this a control monkey was inoculated with the spinal cord. Although this animal did not develop any complete paralysis it was quite distinctly weak in the hind legs and the spinal cord showed a widespread, degenerative change of the nerve cells.

It may therefore be justifiable to regard the disease of this monkey as poliomyelitis. Also the buccal specimen, obtained on the 30th day, gave rise to poliomyelitis in the inoculated monkey. The animal injected with the buccal specimen from the 190th day, on the other hand, showed no symptoms.

#### *Case XXVI. Gösta E—t.*

On Oct. 16 the buccal cavity and intestine were washed.

Of the specimen from the *mouth* 100 c. c. were, on Oct. 19, injected into *Macacus cynomolgus* no. 88. The animal remained well.

Of the *intestinal* specimen 100 c. c. were on the same day injected into *Cynomolgus hamadryas* no. 89. The animal died two days later. The spinal cord showed hyperaemia, solitary haemorrhages, hardly any distinct cellular infiltration; hypertrophy of a great number of the glia cells; degeneration of the nerve cells and commencing glia-cell-neuronophagias. A *Macacus rhesus* that was inoculated with an emulsion of the spinal cord became almost completely paralytic in both hind legs after three days, and died on the fourth day. The microscopic examination showed considerable changes in the spinal cord.



Another washing of the boys mouth and intestine was performed on Oct. 26, the *12th day* after the beginning of the illness.

Of the specimen from the *mouth* 100 c. c. were, on Nov. 2, injected into *Macacus rhesus* no. 119. Nov. 6—10, climbs less lively than usually. Nov. 11, is at first very lively and runs quickly, but after having been running for a while, it is much slower and more careful in its movements. Nov. 15, climbs slowly, respiration panting. Nov. 17, climbs badly and with exertion, appears to be weak in the hind legs. Nov. 19, is sitting huddled up, respiration still panting, diarrhoea. Nov. 20, looks still worse, is sitting huddled up on the floor of the cage, does not like to walk, no isolated paralysis; died in the afternoon.

Moderate hyperaemia of the surface of the brain, the cortex somewhat reddish. The superficial vessels of the spinal cord only slightly injected, on section the spinal cord does not swell, the grey matter is slightly reddish in the cervical and dorsal cords. Recent pneumonias in the lower lobe of the left lung and in the lower posterior portions of the upper lobe, corresponding to these places a fibrinous coating on the surface. Microscopic examination: Slight hyperaemia, no haemorrhages and no cellular infiltration, in some of the vessels a rather large number of white blood corpuscles, hypertrophy of the glia cells and degeneration of a great number of the nerve cells, which are shrunken, deeply stained and coarsely granular, a small number being slightly notched by the surrounding glia cells; commencing karyolysis of the nuclei.

The *intestinal* specimen, 100 c. c., was, on Nov. 2, injected into *Macacus rhesus* no. 120. Nov. 19, looks bad, cyanotic and weak, when running and climbing the animal limps somewhat in the left hind leg. Nov. 20, hoarse, very weak, walks with slow steps, but without showing any isolated paresis. In the evening the animal is lying on the floor and is only with difficulty able to get up. Nov. 21, prefers sitting huddled up, is weak in the hind legs and the gait limping. Nov. 23, climbs with great exertion, runs reelingly and is easily pushed over. Nov. 24, in the evening, is lying on the floor of the cage, moving but very little. Nov. 25, dead.

The brain and its membranes without macroscopical change, the vessels over the spinal cord rather indistinct. On section the spinal cord swells very much, and the grey matter is

somewhat reddish. In the lower lobe of the left lung a small pneumonia. Microscopic examination: Moderate hyperaemia and oedema but no cellular infiltration, distinct hypertrophy of the glia cells and degeneration of a great number of the nerve cells, which are deeply stained and homogeneous with commencing karyolysis of the nuclei; numerous and far advanced glia-cell-neuronophagias.

With an emulsion of the spinal cord, filtered through a Heim, an inoculation was made, on Nov. 29, into *Macacus rhesus* no. 214, both intraperitoneally and into one sciatic nerve. The animal remained well.

The boy was subjected to a third washing of the mouth and intestine on Nov. 12, *30 days* after the onset of the disease.

The specimen from the *mouth*, 12 c. c., was, on Nov. 16, injected into *Macacus rhesus* no. 152. It died on Febr. 12 of tuberculosis of the lungs, liver, spleen and peritoneum, without ever having exhibited any symptoms of paralysis or signs of muscular weakness.

Of the *intestinal* specimen 100 c. c. were injected, on Nov. 16, into *Macacus rhesus* no. 151. The animal died  $2\frac{1}{2}$  months later of a disseminated tuberculosis of the internal organs.

On April 25, *192 days* after the onset of the illness, the last washing of the mouth and intestine of the boy was performed.

The specimens were injected into the *Macaci* nos. 269 and 270, each monkey receiving 100 c. c. Neither of the animals showed any symptoms of disease during the period of observation extending over more than three months.

The examination of the secretions from the boy have proved, that still 12 days after the onset of the illness, he harboured virulent microbes of infantile paralysis on his mucous membranes. In the specimens obtained later on their presence could, on the other hand, not be demonstrated.

Also one of the *abortive cases* previously reported has been examined in the same manner as those exhibiting distinct symptoms of the disease, in order to

ascertain the length of time during which the virus remains on the mucous membranes.

### Observation II. *Ingeborg H—d.*

The first washing of the mouth and intestine was performed on Oct. 19.

*Macacus rhesus* no. 156 were, on Nov. 17, injected with 100 c. c. of the specimen from the *mouth*, but showed no symptoms.

Of the *intestinal* specimen, 65 c. c., was, on Nov. 6, injected into *Macacus cynomolgus* no. 131. On Nov. 8 the animal did not run as quickly as before and seemed to have some difficulty in raising the body by the arms.

On Febr. 3, 112 days after the girl was taken ill, another washing of the mouth and intestine was performed on her.

The specimen from the *mouth*, 140 c. c., was, on Febr. 7, injected into *Macacus cynomolgus* no. 249. Febr. 10, the animal was found on the floor of the cage, making only very slight movements. It died in the evening.

The brain is of ordinary aspect, the surface of the spinal cord, on the other hand, moderately hyperaemic. On section the spinal cord does not swell, the grey matter is distinctly marked, and in the lumbar enlargement of a greyish-red tint. Microscopic examination: Hyperaemia and haemorrhages, but no cellular infiltration; the glia cells as a rule not changed, but the majority of the nerve cells are homogeneous, deeply stained, shrunken and sometimes vacuolated with commencing karyolysis of the nuclei; only a few glia-cell-neuronophagias.

Of the *intestinal* specimen 120 c. c. were, on Febr. 5, injected into *Cercopithecus sabaeus* no. 248. Febr. 12, the animal prefers being on the bottom of the cage but runs and climbs normally; in the evening it is distinctly weak in the hind legs, especially the right. Febr. 13, moves very slowly and carefully, is unable to get up properly on the hind legs when walking, the tips of the toes sometimes being dragged. Febr. 14, is unable to get up on the hind legs, drags the toes in walking. Febr. 17, is sitting with the back curved, does not like to walk, falls now and then and

finds great difficulty in getting up; the patellar reflexes are present on both sides, but less lively than usually. Febr. 18, dead.

The surface as well as the substance of the brain rather congested. The same applies to the surface of the spinal cord, the section is swollen, and the grey matter is distinctly red, mostly in the lumbar region, a slight fibrinous coating over both lungs. Microscopic examination: Hyperaemia, solitary haemorrhages, perhaps a slight degree of cellular infiltration in the grey matter; distinct hypertrophy of a small number of the glia cells; intense degeneration of most of the nerve cells which are changed into irregular, deeply stained, homogeneous and vacuolated lumps of protoplasm, without processes and generally with only an indistinct trace of a nucleus; in some places the surrounding glia cells have eaten their way into the changed cells of the anterior horns.

Both of the monkeys injected with the specimens collected  $3\frac{1}{2}$  months after the time when the girl was unwell, were taken ill and died. The animal inoculated with the intestinal fluid exhibited a distinct paresis of both hind legs, but in the other monkey no paralyses were observed. The microscopic examination showed considerable changes of the ganglion cells in the spinal cord of the first mentioned monkey, less considerable ones in that of the latter animal. Both animals have consequently died of experimental poliomyelitis, which shows that this girl who had presented only very slight symptoms of infantile paralysis, more than three months after their complete disappearance still was a carrier of the virus of the disease.

\*            \*            \*

A summary of the result of these attempts to determine, how long the virus remains on the mucous membranes of persons having suffered from poliomyelitis, is found in the following table.



Table III.

	1:st week		2:nd week		3:rd week		4:th week		5:th week		7:th week		8:th week		4:th month		6:th month		7:th month	
	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.	Mouth	Intest.
Ingrid S—g . . .	+	+	—	—	—	—	+	+	+	+	—	—	—	—	—	—	—	—	0	0
Sigrid Maria R—g	—	—	0	+	—	—	0	—	—	—	+	0	—	—	—	—	—	—	+	0
Erik Wilh. N—g	—	—	0	+	+	0	—	—	—	—	—	—	+	+	—	—	+	+	—	—
Elsa N—g . . . .	+	+	+	+	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—
Harry R—m . . .	+	—	+	?	—	—	—	—	—	—	—	+	—	—	+	?	—	—	—	—
Astrid L—n . . .	0	+	+	+	—	—	—	—	?	+	—	—	—	—	+	0	—	—	—	—
Erik S—m . . . .	+	+	+	0	—	—	—	—	+	0	—	—	—	—	—	—	—	—	0	—
Gösta E—t . . .	0	+	?	+	—	—	—	—	?	?	—	—	—	—	—	—	—	—	0	0
Ingeborg H—d .	0	+	—	—	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—

From this it will be gathered, that *the secretion from the mucous membranes of the mouth and intestine of persons who have recovered has had the power of infecting monkeys still several months, in one case 204 days (nearly 7 months), after the onset of the illness, giving rise to an experimental poliomyelitis with fatal issue.* It cannot very well be denied that a possibility of an infection also of human beings through these secretions must exist. It was only in one case that we did not succeed in demonstrating the presence of the virus after the comparatively short time af 30 days. The subsequent examination of this case at the end of 190 days gave still a negative result. It seems therefore possible that the organism in solitary cases relatively quickly gets rid of the infectious agent or that this at least passes into a non-virulent stage.

During the time occupied by the investigations, the virus had changed its character, so that it no longer caused inflammations with cellular exsudations. Instead of this the degeneration of the nerve cells,

the changes of the glia cells and the neuronophagias caused by the enlarged glia cells have been the characteristic changes. They have thus been of the same type as those appearing in the monkeys injected with secretions from abortive cases and virus carriers, changes which, as will be shown later on, we consider ourselves justified in assuming to be due to a less virulent virus. *The experiment also shows, that the microbe rather quickly — already after 8—14 days — loses its power of causing inflammatory exsudations in the inoculated animals. This fact is of very great importance from a practical point of view since it perhaps gives us right to assume that the virus, possibly rather soon after the termination of the acute stage, gets weaker.*

From what has been said above, it is quite obvious that, practically considered, it would be impossible to isolate convalescents after infantile paralysis sufficiently long, that they might be considered free from the contagion.

As, however, there seems to be reason for assuming that the virus very soon becomes diminished in verulence it is suitable and quite justifiable to keep the patients isolated still for some time, e. g. some weeks, after the disappearance of the acute symptoms. Through this arrangement the advantage would be obtained, that in those cases where the infection really was transmitted, slighter forms of the disease would ensue.

- e) On the strength of proof of the investigations now described and on the possibility of a spontaneous infection of monkeys.

In order to consider the investigations recorded above as evidence, it is necessary to show, firstly, that

a spontaneous infection of the monkeys can be excluded, and secondly that the disease, occurring after the injection of the secretions, can with certainty be assumed to be poliomyelitis.

In the beginning when the number of our experimental animals was not so large, their isolation could be quite satisfactorily effected. Thus, with regard to a great number of the monkeys that were injected with the specimens obtained from dead bodies, the possibility of a spontaneous infection may with certainty be excluded. Later on, owing to want of space and the limited number of cages, it became necessary to keep several monkeys in the same cage, on account of which an infection of healthy animals from those already attacked would be conceivable. We have tried to reduce this risk to the smallest possible by means of immediate isolation of the animals in separate cages apart from the others, as soon as any symptoms of disease were observed. As the virus has always been introduced into the interior of the organism, and in most of the experiments even directly into the nervous system, the assumption seems justified, that as a rule it would reach the spinal cord and the brain and produce symptoms of disease just as quickly as it would penetrate the mucous membranes and get into the secretions and excretions. It may therefore be considered as very probable that in most cases, at least, we have been able to remove the infected animals before they had time to become a dangerous source of infection. Some of the animals, it is true, have had an unusually long period of incubation, so that on this account one might be liable to suspect a spontaneous infection. The *Macacus* no. 163, e. g., which was inoculated with Erik N—g's intestinal specimen from the 52nd day,

was not attacked by the disease and did not die until 5 months after the injection (page 141). When taking into consideration that, as later investigations proved, the boy at the time when the specimen was taken was, still a virus-carrier, the virus was in all probability introduced into the monkey through the injected fluid in question, on account of which a certain degree of immunity ought to have ensued, if the monkey had overcome this infection without any symptoms. Under such conditions the animal would have resisted the infection better than normal monkeys, these latter evidently only with difficulty becoming infected spontaneously. The apparently long period of incubation might be explained by supposing a relapse, the first attack having in this case been overlooked, or so slight, that it had not given any visible symptoms. These conditions will later on be further discussed in connection with the clinical symptoms of poliomyelitis in monkeys.

In order to get some idea of the magnitude of the risk for spontaneous infection under the conditions mentioned, we have, as previous investigators have done, placed healthy monkeys in the cages, occupied by the infected animal. Although several of them remained there for more than a month, no spontaneous infection was observed. A rather robust monkey died, it is true, after an 8 days' stay amongst the infected animals. The grey matter of the spinal cord showed, even macroscopically, a redness, which gave the impression of poliomyelitis, especially as no other changes were found. The microscopic examination showed that although not all the ganglion cells were quite normal, the changes nevertheless could not be considered as due to poliomyelitis. A control inoculation with the spinal cord gave also a negative result. That a spontaneous



infection of monkeys really is possible has lately been demonstrated by LEVADITI and DANULESCO, but to bring about this a great quantity and a high virulence of the infectious material is necessary. We thus consider that the possibility of a spontaneous infection of our animals having taken place is very small. Should it, however, against our supposition, have occurred some time or other, the number of our cases of successful infections would only be reduced by a small percentage. And besides, some of the monkeys employed in our further investigations have been isolated in a satisfactory manner.

The changes found in the spinal cords of the dead monkeys have, even if distinct cellular infiltrations have often been absent, generally been considerable and in most cases sufficient to explain the fatal issue. On the other hand it may be questioned whether they have been sufficiently characteristic to confirm the diagnosis of poliomyelitis. Degenerative changes of the ganglion cells are found not only in epidemic poliomyelitis but also in other infectious diseases in man, e. g. in typhoid fever, acute pneumonia and influenza. In the first mentioned disease there is not only degeneration of the ganglion cells of the brain but also an immigration of leucocytes into them, i. e. neuronophagias, as well as cellular infiltration around the vessels. Consequently we have deemed it necessary to try to ascertain if the changes observed in the monkeys used for our experiments could also occur in connection with spontaneous diseases in monkeys, all the more as the exsudative infiltrations have not been found in any considerable number of our cases.

Our stock of healthy monkeys was sometimes reduced by death of the animals from other causes. Some

of the animals were attacked by diarrhoea, others again looked unwell without giving cause for suspecting any special disease. We have during our investigations always tried to avoid employing such weak specimens. Some of the animals recovered, others succumbed. Sometimes the autopsy revealed acute pneumonia but often there were no changes present, or at least none could be observed other than those due to the diarrhoea. We have also subjected the spinal cord from the naturally dead monkeys to a microscopical examination. The result offers much of interest. The spinal cord of the monkeys which died of *pneumonia* often showed a rather considerable degree of hyperaemia of the grey matter but no haemorrhages. There was almost always to be found a distinct *degeneration of a great number of the ganglion cells*, evident by karyolysis, disappearance of the tigroid substance, shrinking, deep staining and vacuolisation of the protoplasm. The changes were often as far advanced as those found in the injected animals. *On the other hand neuronophagias were, as a rule, entirely absent, or else they were rare and but little advanced. The glia cells were, likewise, as a rule, not hypertrophied.*

In the other monkeys, which died after a protracted diarrhoea or without signs of any distinct illness, the ganglion cells were rather well preserved and the tigroid substance as a rule rather distinct. Sometimes *commencing karyolysis* was noticed and some of the ganglion cells were slightly eroded by surrounding, hypertrophied glia cells. A marked hyperaemia was very rare and haemorrhages have not been found. *The neuroglia cells were as a rule not enlarged.* The monkeys belonging to this latter group consequently did not show any changes that had great similarity to those found in the

animals injected, but the monkeys of the first kind could easily mislead. On this account we have endeavoured to exclude such monkeys as were attacked by pneumonia from our tables, and have included only a few such cases where the pneumonia was minute and very recent.

Amongst the non-injected monkeys none died of tuberculosis. Nevertheless those of the injected animals that were suffering from advanced tuberculosis have also been excluded.

As we have succeeded by means of injected specimens of secretions from a relatively great number of persons to induce clinical symptoms and pathological changes similar to those found in experimental poliomyelitis, the thought is near at hand, that the former have been, at least partially, due to some very common organism that has nothing to do with infantile paralysis or that the microbe of infantile paralysis perhaps is a very common microorganism which perchance is found present in almost anybody.

Although preceding investigations made by other experimentators by no means favour such a supposition we have, nevertheless, in order to settle this question, made investigations on some perfectly healthy individuals with regard to whom we had no suspicion that they had been in contact with persons attacked by infantile paralysis. The only difficulty was to find such individuals in our city, where a large number of cases of infantile paralysis had already occurred. For that reason we had resourse to the Public Orphanage in Stockholm. At that time no cases of this disease had occurred in that institution and the contact with other parts of the town is not very intimate. Through the courtesy of Prof. Medin we have had the opportunity of

examining specimens obtained by washing the mouth and intestine of five children. Three of them were under one year of age, one was  $3\frac{1}{2}$  years and one was 11 years old. All of them were perfectly well. Two of them had only been fed by the breast. The oldest one had spent the summer on Öland, in a place where there had been no case of infantile paralysis. The filtered specimens were, as before, injected into monkeys, into the peritoneal cavity and one sciatic nerve. The animals were then isolated in a room having no communication whatever with that in which the others were kept, and observed for two months. As far as could be ascertained they remained perfectly well during the whole time. One of them died of tuberculosis some time afterwards, the others were employed for investigations with irrigation fluids obtained from cases of infantile paralysis or with passage-virus. They now got ill, became paretic and showed changes of the spinal cord similar to those in other infected monkeys. Nor have we, succeeded in demonstrating the presence of the virus of infantile paralysis in all the persons which have been subjected to an examination in this respect. The specimens from five persons suffering from an undecided illness, but without any contact with cases of infantile paralysis, had no effect on the monkeys injected therewith.

Thus, if those animals that have presented more considerable pathological changes of some other nature are excluded, *and regard is taken for the clinical symptoms presented by the injected animals and, in cases where the pathological changes in the spinal cord are only slight, their nature is verified by means of control inoculations, we are of the opinion that the injected animals are able to give a reliable evidence in a positive direction, even if infiltrative exsudations are not found in the spinal cord.*



From the pareses observed during life in the inoculated animals, no far-going conclusions should according to our experience, be drawn.

Compared with that of previous investigators the result of our experiments are remarkably favourable. The reason why this should be is not very easy to discover. It might possibly be due to the circumstance that we have made use of less tight filters, but this is undoubtedly not the only explanation. We have also obtained positive results with fluids that were filtered through a Berkefeld and even with such that had been passed through both Heim and Berkefeld. Nor can the quantity of the injected fluid have been the essential factor as ROSENAU, SCHEPPARD and AMOS have injected equally large quantities of the irrigation fluids without obtaining a single positive result. Possibly the difference may be due to the fact that we have had the good fortune to discover a strain of the infective agent of exceptionally intense virulence.

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## II. Experimental investigations with the object of determining the possibility of transmission of Infantile Paralysis by means of dead objects and by flies.

By

*Arnold Josefson.*

By what ways the infection of Heine-Medin's disease (Epidemic Infantile Paralysis) takes place cannot yet be regarded as finally settled. It is true, there are some very important facts now known which lead us to believe in a direct transmission of the virus. The propagation of the infection by so called »virus-carriers» has also been suggested, and, according to the above investigations of KLING, PETTERSSON and WERNSTEDT, it has been proved that certain persons exist who harbour the virus of poliomyelitis, although they are themselves clinically perfectly healthy. In spite of the fact that many, let us say the majority of circumstances support the view of a direct infection, upon which also WICKMAN has laid great stress,<sup>1</sup> it has always been held against this view, that, strange to say, neither nosocomial infections nor cases of infection amongst nurses or attendants have been recorded. During the epidemic in Sweden in 1911 in which more than 3000 cases of infantile paralysis

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<sup>1</sup> Studien über Poliomyelitis. Berlin 1905.

were observed, it only occurred once, as far as is known, that any of the nurses became infected. Since it is of importance to publish all such cases, I shall here briefly record the instance:<sup>1</sup>

»E. F., a nurse, had during the summer looked after a case of poliomyelitis in Uppsala. On Sept. 1 she came to Ystad and, on Sept. 19, reported herself ill, after an indisposition lasting a week. She died on Sept. 20 of typical poliomyelitis. In the town of Ystad there had occurred up to that time only two known cases of poliomyelitis. The nurse had not been in contact with either of these two patients nor with their families.»

In Christiania (Norway) two similar cases occurred, in which nurses became attacked by poliomyelitis and died. The nearer circumstances connected with these cases are related in a letter to me by the Chief Physician, Dr. Aaser. He writes: »In all probability both were infected in the Epidemic Hospital. One of them, on returning from her summer holidays, spent in a place where no poliomyelitis occurred, was set to nurse a patient seriously ill with poliomyelitis. After one week she herself was attacked by the same disease and died within 3—4 days. The second nurse was attacked about 4 weeks subsequently to nursing several patients suffering from poliomyelitis. In the meantime she had not been outside the Hospital, but had been attending during this time only scarlet fever patients.»

From the beginning it has seemed to me extremely probable that in poliomyelitis, as in other infectious diseases, the infection could also be transmitted by dead objects.

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<sup>1</sup>. From a letter to the writer by the Chief Physician, Dr. von Wachenfeldt, in Ystad.



No experimental investigations, as far as I know, having been made in this direction up to that date, I decided to investigate the matter as soon as possible. At the Epidemic Hospital of Stockholm, through the kindness of the Medical Superintendent, Dr. Hellström, I had an opportunity of collecting some material. To ascertain whether the virus could possibly adhere to dead objects I gave a girl and a boy, both of whom were severely affected, each a compress to be used as a handkerchief for a week. Further I let a girl who was seriously ill do some fancy work on a piece of paper and let a picture book circulate among the children. Besides this, I asked the patients to catch flies in the wards. Prof. A. Pettersson has kindly placed the necessary monkeys at my disposal and enabled me to submit the collected material to an experimental investigation. I would at the same time express my indebtedness to Prof. Pettersson for not only having followed my work with great interest but also having at all times, more especially at the microscopic examination of the sections, kindly given me the benefit of his great experience.

I began the experiments in the month of September 1911 and on Nov. 27, before the Association for Internal Medicine, I showed a monkey with distinct symptoms of poliomyelitis (Case 1), which had been infected by me with an extract of the handkerchiefs. At this meeting<sup>1</sup> I also gave a report of my other investigations.

In my experiments I have always tried to imitate nature as far as possible.<sup>2</sup> The objects had been in pro-

<sup>1</sup> Allm. Svensk. Läkaretidn., Dec. 1911.

<sup>2</sup> The well known experiment by Flexner, Clarke (Journ. of Amer. Med. Assoc. Vol. LVI, 1911 <sup>10</sup>/<sub>6</sub>), who produced experimental poliomyelitis

longed contact with the poliomyelitis patients. Afterwards they were kept in empty, sterile vessels for some days (natural drying) before I put them into physiological saline solution. Experiments were made with this saline washing fluid at the end of varying lengthy periods of time. (The flies were not ground up). Immediately before an injection the fluid was filtered through a Heim asbestos filter, which method has been shown to be best through the investigations of KLING, PETTERSSON and WERNSTEDT.<sup>1</sup>

In most of my experiments the filtrate was injected both intraperitoneally and intraneurally (sciatic nerve) into monkeys. The injection was made under æther anaesthesia.

The spinal cord of the infected monkeys was always reinoculated into control-animals.

In order to avoid sources of error the infected monkeys were isolated in smaller cages.

All the spinal cords were examined microscopically.

### *Experiments with handkerchiefs.*

I. *Macacus cynomolgus*. On Oct. 16, 1911, 45 c. c. of a 2 days old extract of the handkerchief belonging to the boy H. were injected intraperitoneally and 1 c. c. intraneurally. Oct. 19, the animal seems to be weak in the left hind leg. (The injection was made into the left leg.) Oct. 24, still weak in left hind leg. Oct. 27, moves normally. Nov. 11, rather slow in its movements. Nov. 15, the monkey undoubtedly weak in left front and hind legs and unsteady on the right hind leg. Seems ataxic. Nov. 17, the pareses are more distinct. Nov. 20, condition unchanged. Nov. 24, weak in both hind legs. Nov. 25, almost complete paralysis of the right

by means of flies, which had been allowed to walk on the spinal cord of poliomyelitis-patients, is no imitation of the conditions with which we have to do in practice.

<sup>1</sup> Zeitschr. für Immunitätsforsch. u. exp. Ther., 1912 p. 317.

fore leg. Nov. 27, the animal is now weak also in the left fore leg. Movements ataxic. The monkey is demonstrated before the Association for Int. Medicine. Nov. 28, lying motionless in the cage. Nov. 29, dead.

At the autopsy no macroscopic changes were found in the spinal cord and brain. The internal organs called for no remark.

The microscopic examination of the spinal cord showed moderate hyperaemia, haemorrhages in the grey matter, no infiltration either in the meninges nor in the spinal cord. The cells of the supporting tissue enlarged, showing transparent, clear, non-stained cell-bodies without visible processes. The nucleus was here generally deeply stained and rich in chromatin. The ganglion cells were, as a rule, more or less degenerated, shrunken, homogeneous and mostly deeply stained; some of the cells vacuolated. The nucleus as a rule, deeply and diffusely stained. Other ganglion cells were very pale, finely granular and seemed to be without any processes. These cells showed a pyknotic nucleus. In the anterior horns the cells of the supporting tissue nearest the ganglion cells were observed in great numbers to have eaten their way into the latter, forming more or less deep notches in the deeply stained cell bodies, these indentations being occupied by the pale phagocytes. At times there remained of the whole ganglion cell nothing but a star-shaped, amorphous, diffusely stained mass. Here and there the changed ganglion cells were surrounded by palissade-like rows of cells from the supporting tissue. The changes were most marked in the cervical cord.

An emulsion of the spinal cord was injected into a control monkey on Dec. 1, 1911. No motor symptoms. The animal died, on Dec. 28, of tuberculosis of the lungs (chronic and acute). The spinal cord very hyperaemic.

II. *Macacus rhesus*. Nov. 7, 1911. Intraperitoneally 60 c. c. and intraneurally 1 c. c. of a 1½ week old extract from a handkerchief belonging to the girl S. R. The secretions of this girl were examined by Kling, Pettersson and Wernstedt (case XVII).

Nov. 19, the animal died without having exhibited any symptoms of poliomyelitis.

The spinal cord, brain and their membranes vividly hyperaemic. The substance of the spinal cord swelled on section. Double-sided pleuro-pneumonia. On microscopic examination the spinal cord

showed a very marked hyperaemia; the ganglion cells remained unchanged.

### *Experiments with the picture-book.*

*Cercopithecus Burnetti.* Oct. 19, 1911. Intraperitoneally 80 c. c. and intraneurally 1 c. c. of a 5 days old washing fluid. Great effect of the anaesthetic (artificial breathing). Oct. 20, slow in most movements looks ill. Oct. 24, somewhat less slow. Oct. 27, moves but little, runs badly. Oct. 28, seems to be weak in the hind legs. Oct. 30, dead.

The autopsy showed marked hyperaemia of the spinal cord, the whole substance looking hyperaemic. The internal organs showed no changes. On microscopic examination small haemorrhages and hyperaemia in the spinal cord; otherwise no changer.

Control animal A. *Macacus rhesus.* Only intraneurally 1 c. c. of an emulsion of the spinal cord. No symptoms; survived.

Control animal B. *Cercopithecus.* Intraperitoneally 10 c. c. and intraneurally 1 c. c. Died after two days. A *Macacus rhesus* was infected with the spinal cord of this animal. Died on the fourth day of double pneumonia. The spinal cord showed no changer.

### *Experiments with fancy-work.*

*Macacus cynomolgus.* Oct. 19, 1911. Of a 5 days old extract of the fancy work previously mentioned 75 c. c. were injected intraperitoneally and 1 c. c. intraneurally. Great effect of the anaesthetic. Oct. 20, less lively. Oct. 22, still more slow, weak in the left fore and right hind leg. Oct. 24, is sitting motionless; does not eat. Oct. 27, the right hind leg paralytic, the left leg weak. Oct. 28, marked paresis of the left fore and both hind legs. Oct. 30, dead.

The autopsy revealed no macroscopic changes. On microscopic examination the spinal cord showed slight hyperaemia, slight cellular infiltration in the neighbourhood of the central canal, neuronolysis and destruction of the ganglion cells in the same manner as in case I.

Control animal A. *Macacus rhesus.* Intraneural injection of an emulsion of the spinal cord. No symptoms; survived.



On June 1912, this monkey together with some other previously not injected animals was inoculated with passage-virus into one sciatic nerve. Although the others died of experimental poliomyelitis this monkey resisted the attempt at infection. Thus it is probable that this latter monkey, through the previous injection with spinal-cord-emulsion from the *Macacus cynomolgus* which had been injected with fancy work extract, had acquired a certain immunity. This makes it extremely probable that this needle-work-extract injected monkey had suffered from poliomyelitis.

Control monkey B. *Macacus cynomolgus*. Nov. 11, 1911. Intraperitoneally 7 c. c. and intraneurally 1 c. c. of the above mentioned emulsion of the spinal cord. The animal died of bronchopneumonia and enteritis after 15 days. The spinal cord hyperaemic; microscopically no changes in the ganglion cells.

### *Experiments with flies.*

I. *Macacus cynomolgus*. 40—50 of the flies that had been kept in saline solution were now ground up with sand and again shaken in saline solution. The whole mixture was filtered and immediately injected intraperitoneally (30 c. c.) and intraneurally (1 c. c.) on Oct. 5, 1911.

The monkey died on Dec. 4 without having shown any signs of poliomyelitis.

The autopsy revealed double-sided adhesive pleurisy and enlargement of the spleen. Slight redness of the spinal cord.

Control animal. *Macacus cynomolgus*. Emulsion of the spinal cord, 20 c. c. intraperitoneally, and 1 c. c. intraneurally, on Dec. 1, 1911. Dec. 7, seems to be ill. Dec. 8, climbs badly, the left fore leg weak. Dec. 9, almost paralytic in the left fore leg. Dec. 10, dead.

In the liver and the diaphragm small greyish-white tubercles; the lungs normal. The spinal cord perhaps a little reddish. Microscopically no change other than hyperaemia.

II. *Macacus cynomolgus*. 20—30 flies kept in NaCl during 1½ weeks. Filtration and injection of resp. 25 c. c. and 1 c. c., on Nov. 7, 1911. Deep anaesthesia; artificial breathing. Nov. 13, climbs unwillingly. Nov. 16, weak in the hind legs, especially the left one. Falls and has difficulty in getting up again. Nov.

17, very weak in the hind legs; has grown thin. Nov. 20, still worse. Nov. 23, still very weak in the hind legs. Nov. 24, dead.

Marked hyperaemia of the membranes of the spinal cord and a slight redness of the cord itself. On section the spinal cord rather moist, did not swell. Microscopically no changes other than hyperaemia and haemorrhages.

A control monkey died after 27 days of acute and chronic tuberculosis of the lungs.

By the experiments now recorded it is demonstrated that the virus of poliomyelitis can adhere to dead objects (handkerchiefs, fancy work) and in a dried state remain virulent, as has also been assumed by other investigators. The changes in the spinal cord do not, it is true, reveal the ordinary aspect; we notice especially the absence of any cellular infiltration. On this point the investigations of KLING, PETTERSSON and WERNSTEDT have thrown a new light by showing, with the help of a larger material, that degenerative changes alone, similar to those described above, may be found in monkeys suffering from undoubted poliomyelitis, that is to say, infiltration need not necessarily be present.

On the question of the resistance of the virus of poliomyelitis to the process of drying opinions differ somewhat at present. While RÖMER<sup>1</sup>, FLEXNER and LEWIS<sup>2</sup>, LANDSTEINER and LEVADITI find it resistant for several days, LEINER and v. WIESNER are of the opinion that such is not the case. They found that when the virulent material was allowed to dry slowly in a thin layer it became non-virulent within 4—24 hours. The secretion had in both of my positive cases in all probability existed only in a thin layer on the handkerchief and the fancy-work.

<sup>1</sup> Römer, *Die epid. Kinderlähmung*, 1911 p. 89.

<sup>2</sup> *Journ. of the Amer. Med. Ass.*, L. III, 1909.

ZAPPERT. v. WIESNER and LEINER write: A transmission of poliomyelitis through dead, infected objects is not very probably, as the virus of infantile paralysis, according to our experience, is soon destroyed by drying.»

E Müller<sup>1</sup> writes: »That lifeless material, especially milk or drinking water, should spread the disease further is hardly probable. . . Renewed investigation is demanded, however, for the solution of the question whether the transmission of the virus from one person to another could not take place through the medium of some animal organism». (Both of my fly-monkeys gave a negative result).

He says, further: »The contagion might be transmitted indirectly thereby, in that the virus present in such discharges (gastro-intestinal evacuations, saliva spectrum) might be transmitted to food and articles in common use (clothes, shoes etc.) and spread through them. These are, however, but riddles and can be solved only through later experimental investigations.»

LANDSTEINER, LEVADITI and PASTIA<sup>2</sup> have made investigations with regard to the length of time during which the virus remains potent in sterile milk or sterile water. This is found to be (at ordinary room temperature and light) at least 31 days.

That I was enabled to succeed in producing experimental poliomyelitis with a handkerchief and fancy-work, is in the light of KLING, PETTERSSON and WERNSTEDT's now published investigations, quite natural. After I had commenced my investigations and made

<sup>1</sup> Handbuch d. inn. Mediz., 1911 p. 804.

<sup>2</sup> Annales de l'inst. Pasteur, 1911, p. 805.

a preliminary report to the Assoc. for Int. Medicine I found an experimental investigation which fully confirmed my results. NEUSTÄDTER and THRO<sup>1</sup> had collected dust from rooms in which poliomyelitis patients were warded, and infected monkeys with it. In this way they could produce poliomyelitis, and this even in further passages.

In both my positive cases (handkerchief, fancy work) I tried to re-inoculate the virus, but, I am sorry to say, the animals died from other causes.

*My experiments have thus demonstrated that the virus adheres to lifeless objects and can remain virulent, but I was unable to show this in the case of flies.* It had been my intention to look for the presence of the virus in food that had come into contact with patients, but, on account of other causes, I was unable to carry this into effect.

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<sup>1</sup> New York Med. Journal, 1911, No. 17.





### III. Some conclusions with regard to the manner of dissemination of the infection based upon our investigations, and concerning the possibility of a transmission of the infection by means of blood-sucking animals.

By

*Carl Kling, Alfred Pettersson and Wilhelm Wernstedt.*

We have succeeded in demonstrating the presence of the microbe of infantile paralysis on the mucous membranes of the mouth, nose, pharynx, trachea and the intestine of persons who have died of infantile paralysis. We have also done this on the corresponding mucous membranes of typical cases during life, excepting in the case of the trachea, which has not been subjected to an investigation, and we have further demonstrated its presence in the same places in patients who were only very slightly attacked and presented no characteristic symptoms; some of these latter lived in the surroundings of positive cases of infantile paralysis, others again under conditions where, as far as could be ascertained, no intercourse with cases of paralysis had taken place. Finally we have demonstrated the presence of the virus in persons who were themselves perfectly well but had been in contact with cases of infantile paralysis. There occur, as has been pointed

out by WICKMAN, ZAPPERT, MÜLLER, NETTER and others, in times of infantile paralysis a large number of cases that do not show the symptoms hitherto considered as characteristic of this disease. With regard to these the clinical diagnosis cannot with certainty determine the nature of the disease in more than quite a minimal proportion of the cases. To these sources of infection must further be added the existence of an undoubtedly large number of »virus carriers». *Since the microbe is known to exist on the above mentioned mucous membranes in persons who have never been ill, it must be presumed that it has got there from outside and in all probability through infectious secretions from other individuals. Under such circumstances there is no reason for doubting this manner of transmission also with regard to those affected by the disease, no matter whether these are typical or atypical cases.* The presence of the virus on the mucous membranes of the patients must therefore not necessarily be the result of an excretion from the interior of the organism, but may instead be due to a proliferation of microbes which have been transported to the mucous membranes from outside. That the former, a discharge of microbes, so to speak, may take place in man is very probable, since LANDSTEINER, LEVADITI and DANULESCO as well as LEVADITI and DANULESCO have succeeded in demonstrating the existence of the microbe in the nasal mucus of monkeys which had been intracerebrally infected, but how often and to what extent an excretion of this kind takes place is yet quite unknown.

According to our experience the virus-carriers and the abortive cases in a family may be four or five times as numerous as the cases showing typical symptoms. The abortive cases are naturally, in their turn, surrounded by

other abortive cases and virus carriers. Under such conditions it is not surprising that we have up to the present time not succeeded in finding any connection between the different cases. In order to be able to follow the path of the infection some traces of it must first be found and it is just this that has hitherto proved impossible. The picture given by JÄGER of cerebro-spinal meningitis from an epidemiological point of view can with utility be applied also to the case of infantile paralysis. The former disease has hitherto, according to JÄGER, presented itself as a mountainous landscape covered by a dense fog, out of which only the peaks have projected far apart, but as the fog disperses the ridges connecting the peaks also become discernable.

When we discover methods that admit of an etiological diagnosis instead of the symptomatological, the fog now covering the unknown in infantile paralysis will disappear and allow us to see clearly the mode of infection. *Then we shall probably find that infantile paralysis is a common disease of childhood, generally displaying only very slight symptoms, but sometimes acquiring a more virulent character giving rise to disturbances in the nervous system.* The same applies also to other infectious diseases. Scarlet fever, for instance, in certain epidemics, shows an inclination to cause changes in the kidneys or other organs. We shall then perhaps find the circumstance that grown up persons only very seldom are attacked by infantile paralysis explained (as it is in scarlet fever) by the fact that adults have already had the disease in their childhood. Finally we may discover that the reason why greater towns seem to have been relatively spared the disease lies in the fact that the non-malignant form, which we have hitherto never taken into consideration, is,

owing to more lively communications, much more common in the towns than in the country, in this respect resembling a number of other diseases, e. g. measles.

It is probable that the propagation of infantile paralysis can occur also by some other method than by direct transmission of the microbe from person to person. Perhaps it is spread through infected household utensils or clothes. WICKMAN records a case where the infection possibly was transmitted through a sketch. It may also be conceived that certain animals e. g. flies, could possibly sometimes transmit the infection, but no observations have as yet been made with regard to such cases. JOSEFSON in his paper has given evidence in support of the former supposition. LANDSTEINER, LEVADITI and PASTIA have shown that the microbe can remain virulent for 31 days in sterilised milk, and NEUSTÄDTER and THRO have discovered its existence in dust.

WICKMAN has communicated cases which might be suspected to have had some relation to the consumption of probably infected milk. It would perhaps be worth while to draw attention to the possibility of a dissemination through milk, other beverages and food, as well as other articles, such as books, etc.

Infantile paralysis has an inclination to become epidemic in the latter part of the summer or in the early autumn. In this respect it resembles typhoid fever, dysentery and cholera. The cause of this seasonal incidence, still almost unknown, is probably identical in the four diseases. This time of the year usually favours the prevalence of infectious diseases of the intestine, more especially the three diseases just men-



tioned. It is therefore quite natural that the intestinal canal was formerly considered to be the chief point of entrance of the virus of infantile paralysis, all the more as pathological changes in the intestine and its lymphatic glands are almost always found to exist.

*When taking into consideration the circumstances pointed out by us, it must be admitted that there scarcely exist any really weighty reasons to oppose the correctness of the view accepted already by WICKMAN that the disease spreads from one person to another.* This manner of transmission must even be considered as very probable, being also able to explain quite satisfactorily the occurrence of the disease in apparently isolated foci. But the other possibility to which allusion has been made in the beginning of this report, must also be taken into consideration, and the possible function of bloodsucking insects as virus carriers and originators of epidemics of infantile paralysis must be duly investigated.

In order to be able to fully understand the possibilities of a propagation of this kind, it must first of all be remembered, that investigations on monkeys have shown that the microbe must exist only in small quantity in the blood. It is necessary to inject a large quantity of blood into an experimental animal in order to infect it. Further, the microbe can exist in the blood only during the acute stage. By investigations on animals it has been proved that recovery from the illness creates immunity. Experiences from epidemiological observations substantiate this. The disease evades places that have recently been visited by an epidemic and vice versa. In 1905, for instance, the epidemic in Sweden made great havoc in the county of Kronoberg. As will subsequently be shown by WERNSTEDT, only a few cases occurred in this county during last year's

epidemic, in comparison with the numbers of cases in surrounding counties. Experiments on animals have shown that the acquired immunity is an immunity against the microbe and that the protecting elements are present in the blood. It must therefore be presumed that the microbe, owing to the immunity created, disappears from the blood when the acute stage is over. A theory which tries to explain the spreading of the disease by means of a transportation of the microbe from the blood, must always presume the existence of acute cases in order to explain the origin of new ones.

*The presence in the blood of only a small number of microbes and their short existence there would seem to prevent the transmission of the disease from one person to another through blood-sucking insects in the sufficiently great extent necessary to cause real epidemics.* But there exist also other reasons for the non-acceptability of this theory. In order to explain the spreading of the disease over large areas a dissemination must be presumed by animals that are themselves capable of travelling over long distances. On this account it is scarcely possible that a transmission of the infectious agent through the common parasites of man, i. e. fleas, bugs and lice-provided that such transmission really takes place-could give rise to the more extensive epidemics.

There remain to be considered the other insects. Infantile paralysis has hitherto ravaged more especially the northern temperate zone. In this region the insect-life is subjected to considerable variation, owing to the changes in the temperature during the year. The vital functions of the insects being checked by cold, the disease ought also to cease at the approach of winter if its propagation depended upon insects.

In Sweden it has not been possible to find any such correspondance between the seasonal temperature and the prevalence of the disease that the spread of the infection might be attributed to insects. The curve representing an epidemic of infantile paralysis usually reaches its maximum in August or September, declines gradually and seems to be only slightly influenced by the cold of October and November. Small epidemics have occurred which have both commenced and ceased during the winter. In the beginning of this year a rather large number of cases occurred in Kalix, situated in the northern part of Sweden, on the 66th degree of northern latitude.

Malaria was formerly very common in our country. The curve had quite another appearance than that of infantile paralysis. It also reached its maximum in August and September, but the cold of autumn always put a limit to its further progress.

Although the blood-sucking insects evidently cannot be ascribed such a rôle as propagators of the disease that the occurrence of real epidemics could be explained thereby, their possible influence, on the other hand, should not be altogether denied. It might be conceived that they play some part in the origin of house-epidemics, of which a typical case was observed last year in a large tenement house in Stockholm. We have tried by experiments to gain some information also on this point.

In September five fleas were collected from a family in which some persons had been attacked during August by infantile paralysis. These fleas were ground up in a mortar with saline solution and then injected into the sciatic nerve of *Cercopithecus Burnettii* no. 143. The monkey died 13 days later without having shown any distinct pareses. At one autopsy no changes of the internal organs were

found. The slight change observed in the spinal cord viz an inconsiderable degree of degeneration of a small number of the nerve cells could not, in our opinion, be regarded as evidence of poliomyelitis.

Two fleas taken from another case of infantile paralysis were treated in the same manner as in the preceding case and injected into *Cercopithecus Burnetti* no. 161, on November 21. The monkey died on Dec. 21 without having presented any pareses or muscular weakness. The left lung contained several small patches of pneumonia. The spinal cord showed only slight degeneration of a small number of the nerve cells.

In order to be perfectly sure that the fleas contained blood from an organism infected by infantile paralysis, twelve such animals were collected and allowed to suck their fill of the blood from Baboon no. 93 on November 11, the day after the animal was attacked by the disease. After the sucking all the animals were quite full of blood. On Nov. 15 they were ground fine, mixed with saline solution and injected into one sciatic nerve of *Macacus rhesus* no. 146. The monkey died on Nov. 20. During the last two days it had moved slowly, climbed badly and been looking weak. The autopsy revealed swollen and caseating mesenteric and portal glands, tubercles and caseating foci, some of the size of a pea, in the liver and spleen, as well as tubercles in the lungs. In the cervical cord some of the ganglion cells were rather degenerated. — None of the monkeys showed any inflammatory changes at the seat of inoculation into the sciatic nerve.

Thus, in none of the experiments with fleas have we succeeded in inducing experimental poliomyelitis. It must, however, be admitted, that only one of the experiments was pure, as in the other two cases the animals employed were suffering from a secondary infection.

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#### IV. The clinical picture of experimental poliomyelitis in monkeys.

By

*Carl Kling, Alfred Pettersson and Wilhelm Wernstedt.*

The clinical picture of experimental poliomyelitis in monkeys has been described in detail by LANDSTEINER and LEVADITI, FLEXNER and LEWIS, LEINER and v. WIESNER, RÖMER and others. These investigators, in the course of their experiments, have found in the monkey most of the symptoms that can occur in man suffering from infantile paralysis. The experiences hitherto gained are excellently compiled by RÖMER and by LEINER and v. WIESNER in their monographs (1911). It is therefore unnecessary to give here a detailed description of the symptoms which we have observed in our experimentally injected animals, as this would only constitute a repetition of facts already known. Our relatively large material of poliomyelitis in monkeys offers, however, some points that may be worth mentioning, e. g. in regard to the period of incubation, the duration of the disease, its prognosis and mortality. We have also had occasion to observe some types of the disease which hitherto have only

rarely been observed and finally some the occurrence of which has been denied in some quarters.

The material is collected in three separate tables, comprising altogether 120 monkeys. Only undoubtedly positive cases are included, 116 being confirmed by microscopical examination of the nervous system; the remaining four cases survived, but the clinical symptoms in these were quite sufficient to make the diagnosis certain. All animals with secondary infection, such as extensive pneumonia, advanced tuberculosis, etc. are excluded from the tables. Table no. IV comprises 62 monkeys which have been infected with material from typical cases of infantile paralysis or from subjects immediately after death from typical acute infantile paralysis. Table no. V, 35 monkeys which developed poliomyelitis after inoculation with the buccal or intestinal secretions from abortive cases and healthy persons, and finally Table no. VI, 23 animals in which the disease was induced by similar secretions, procured from cases at different periods after the recovery from a typical attack of infantile paralysis.

*The stage of incubation.* LANDSTEINER and LEVADITI in their investigations have generally found a period of incubation varying from 7—11 days, the shortest period observed by them being 4, the longest 23 days. According to FLEXNER and LEWIS the majority of animals are attacked on the 8:th—12:th day, but a considerable number, however, are affected either before or after this average time; in one case the monkey did not develop paralysis until the 33:rd day after inoculation. LEINER and v. WIESNER have once seen the period of incubation prolonged to 46 days. RÖMER has found an average of  $9\frac{1}{2}$  days, the shortest being  $3\frac{1}{2}$  and the longest 15 days.

Table. IV.

Monkeys infected with material from cases of typical infantile paralysis during the acute stage.

M. r. — *Macacus rhesus*, M. c. — *Macacus cynomolgus*, C. h. — *Cynocephalus hamadryas*. C. f. — *Cercopithecus fuliginosus*, C. B. — *Cercopithecus Burnetti*, C. s. — *Cercopithecus sabaeus*, C. r. — *Cercopithecus ruber*, M. f. — *Macacus pileatus*.

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. r. 7	Trachea.	11	13	Paralysis of left leg; on 3rd day paralysis of both legs; last day paralysis of the arms.	+	
M. r. 8	Intestine.	9	5	Paralysis of both arms; 3rd day also of the legs.	+	
M. r. 4	Mouth.	14	survives	Paralysis of right leg, some days later paresis of left hand. Died about 3 months later.		
M. r. 5	Spinal cord from man.	9	survives	Paralysis of right arm.		
M. c. 23	Mouth.	(54)	50	Slow in movements, during the time following progressive muscular weakness.		+
M. c. 22	Trachea.	9	11	Pareses of right arm. Found dead after 11 days.		+
M. c. 55	Spinal cord from No. 22.	7	1	Complete paralysis of right leg.	+	
M. r. 56	Spinal cord from No. 22.	10	4	Complete paralysis of both legs.	+	+
M. r. 18	Intestine.	28	50	Paretic in both legs, increasing weakness during the nearest time following, the last day lying down.		+
M. c. 10	Mouth.	(33)	1	Lying on the bottom of the cage; paretic in all extremities.		+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. c. 11	Trachea.	18	15	Paretic in one of the extremities (trotting); on 11th day distinct paresis of left leg.		+
M. c. 13	Intestine.	3	5	Paretic in the arms, next day in the legs also; on 5th day lying on the bottom of the cage.		+
M. c. 12	Spinal cord fr. man.	13	< 1	Found dead.	+	
M. c. 21	Intestine.	18	9	Very weak; on the 9th day distinct paresis of left arm.		+
M. c. 15	Mouth.	11	< 1	Found dead.	(+)	+
M. c. 14	Trachea.	7	8	Paresis of one leg; later on general muscular weakness.	(+)	+
M. c. 16	Spinal cord fr. man.	15	12	Paresis of one arm; increasing general muscular weakness.		+
M. c. 19	Intestine.	5	1	In the morning paretic in the arms; in the evening lying on the bottom of the cage.		+
M. c. 46	Spinal cord fr. No. 19.	16	4	Paretic in the arms; increasing general muscular weakness.		+
M. c. 39	Spinal cord fr. man.	5	2	Paralysis of both legs.	+	
M. c. 26	Mouth.	5	2	Paretic in the arms; progressive general muscular weakness.	(+)	+
M. c. 47	Spinal cord fr. No. 26.	19	10	Paresis; paralysis of both arms.		+
M. c. 48	Spinal cord fr. No. 26.	3	8	Paresis of both arms; the last day paretic in all the extremities; respiratory paralysis.		+



Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. c. 40	Spinal cord fr. man.	8	9	Paretic in the left arm; later on in both legs.		+
M. c. 31	Mouth.	12	9	Paresis of both arms; later on general muscular weakness.		+
M. c. 30	Intestine.	6	5	General muscular weakness.		+
M. c. 33	Spinal cord fr. man.	21	4	Paretic in both legs; the next day also in one arm; increasing weakness; ataxia.		+
M. c. 29	Mouth.	12	1	Paralysis of both legs.	+	
M. c. 28	Trachea.	3	18	General debility; increasing muscular weakness, especially of the muscles of the trunk; next day lying on the bottom of the cage.		+
M. c. 27	Intestine.	6	2	Paretic in all the extremities; facial and oculo-motor paresis.	+	(+)
M. c. 34	Spinal cord fr. man.	5	6	Paresis of left arm, later on paralysis; paresis of both legs.		+
M. c. 36	Mouth.	21	7	Paretic in the legs. after 4 days paretic in one arm, lying on the bottom of the cage the day previous to death.		+
M. c. 37	Trachea.	5	5	Paresis of both hands; on the 4th day paretic in the legs.		+
C. h. 42	Spinal cord fr. man.	30	3	Paresis of both legs.		+
C. h. 44	Intestine.	7	2	Hands in position of radial paralysis.		
C. h. 50	Trachea.	4	16	Radial paralysis-position of left hand. On 5th day paresis of one leg; on the day before death lying on bottom of the cage.		+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	S y m p t o m s .	Anatomical changes.	
					Infiltration.	Degeneration
C. h. 49	Intestine.	8	?	General debility.		
C. h. 54	Spinal cord fr. man.	2	1	Paresis of left hand.		+
M. c. 25	Mouth.	24	< 1	Lying on bottom of cage, paretic in all extremities; commencing respiratory paralysis.	(+)	+
M. c. 52	Mouth.	7	< 1	Found dead.	+	
M. c. 67	Spinal cord fr. No. 52.	4	2	Paretic in one leg; next day in all the extremities.	+	+
M. c. 68	Spinal cord fr. No. 52.	3	3	Paretic in the legs; on the 3rd day in all extremities.	+	(+)
M. c. 69	Spinal cord fr. No. 52.	6	< 1	Found dead.	(+)	+
M. c. 75	Intestine.	11	4	Complete paralysis of both legs; on 3rd day of all extremities.	+	+
M. c. 78	Mouth.	(70)	< 1	Found dead.		+
M. c. 77	Intestine.	2	2	Paresis of left leg; the next day increasing weakness of the muscles of the legs, arms and trunk.	(+)	+
M. c. 70	Mouth.	17	< 1	Lying on the bottom of the cage, paretic in all extremities; commencing respiratory paralysis.	(+)	+
M. c. 71	Intestine.	23	2	Complete paralysis of left arm, paretic in the legs.	+	
M. r. 76	Intestine fr. No. 71	4	2	Paretic in the left arm, limbs, general debility; dying on the following day.	(+)	+
C. B. 141	Spinal cord fr. No. 76.	12	5	Paretic in right arm; the following days increasing weakness; 5th day, paretic in the legs.	(+)	+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. c. 72	Mouth.	7	2	Complete paralysis of left leg; later in the same day paralysis also of right leg.	+	(+)
M. c. 73	Intestine.	3	3	Paretic in left leg; 3:rd day general convulsions, paralysis of cervical muscles; paretic in the arms.		+
C. h. 93	Spinal cord fr. No. 73	21	4	Tremor, ataxia, convulsions, the following day increased ataxia, cross-tempered, in the evening paretic in legs and right hand; 3:rd day complete paralysis of both legs and arms; left-sided ptosis.	+	(+)
C. B. 140	Spinal cord fr. No. 73.	8	10	Muscular weakness, increasing during the following days; 5:th day, distinct paresis of the arms.		+
M. c. 82	Mouth.	5	< 1	Found dead.		+
M. r. 100	Spinal cord fr. No. 82.	3	30	On the first day after onset: does not climb normally (paresis of the arms?); one month later: a sudden change for the worse, general debility; the next day lying on the bottom of the cage, paretic in all extremities.		+
M. c. 85	Intestine.	4	4	Paretic in left leg; the next day also in the left arm; 4:th day, paretic in all the extremities, right-sided ptosis.	(+)	+
M. c. 83	Mouth.	3	7	General debility; 7:th day, lying on the bottom of the cage, paretic in all the extremities.		+
M. c. 84	Mouth.	3	6	Paresis of both arms; the next day also of left leg.		+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. c. 81	Intestine.	(53)	1	Muscular weakness, especially of the arms.		+
C. h. 89	Intestine.	2	< 1	Lying on the bottom of the cage, parietic in all the extremities.		+
M. r. 99	Spinal cord fr. No. 89.	3	1	Complete paralysis of both legs.		+



Table V.

Monkeys infected with secretion from abortive cases and virus carriers.

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infection.	Degeneration.
M. c. 179	Mouth.	11	19	Climbs badly (paretic in arms?); found dead on the 19:th day.		+
C. f. 178	Mouth.	27	1	Paretic in the legs; does not climb; dies the following day.		+
M. c. 230	Spinal cord fr. No. 178	(43)	1	Lying on the bottom of the cage; paretic in all the extremities.		+
M. c. 131	Intestine.	2	?	Paretic in the arms.		
C. s. 248	Intestine.	7	6	Paretic in both legs; the following days increasing general muscular weakness. Patellar reflexes weak on both sides.	(+)	+
M. c. 217	Mouth.	3	3	Paresis of left arm; 3:rd day, lying on bottom of cage, paretic in all extremities.		+
M. c. 103	Mouth.	3	2	Paretic in the arms, in the evening of the same day also in the legs; dies the next day.		+
M. r. 111	Spinal cord fr. No. 103.	(59)	< 1	Found dead.		+
C. f. 138	Spinal cord fr. No. 103.	11	9	Paretic in left arm. 9:th day, marked paresis of same arm; later in same day lying on the bottom of the cage.		+
M. r. 115	Mouth.	19	20	Climbs slowly (paresis of the arms?); on the 19:th day paretic in the legs, last day lying on bottom of the cage.		+
M. r. 204	Spinal cord fr. No. 115.	7	< 1	Found dead.		+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. r. 106	Mouth.	25	5	Climbs slowly (paretic in the arms?), thin; 3:rd day, marked paresis of the arms, weak also in the feet.		+
C. f. 174	Spinal cord fr. No. 106.	6	1	Lying on the bottom of the cage, paretic in all the extremities.		+
C. f. 203	Spinal cord fr. No. 174.	17	1	Paralysis of the left leg.		+
M. c. 136	Mouth.	3	63	Climbs slowly, jerkingly (paretic in one of the arms?); 61 days after inoculation: condition worse, left hand in paresis-position; general muscular weakness, tremor; died after 2 days.		+
M. c. 133	Intestine.	2	6	Paretic in the legs; 3:rd day also in the arms; 5:th day paralysis of right hand.		+
M. r. 153	Spinal cord fr. No. 133.	3	13	Climbs jerkingly (paresis of the arms?) 12 days after onset, condition worse and on 13:th day paretic in all the extremities.		+
M. c. 135	Mouth.	4	20	Climbs jerkingly (paretic in the arms?); 23 days after inoculation paretic in the hind legs; the next day dying.		+
M. r. 129	Intestine.	23	1	Paretic in the legs.		+
C. s. 202	Intestine.	7	2	Paretic in all the extremities, chiefly in the legs; the day following lying on bottom of cage.		+
C. s. 210	Mouth.	4	2	Paresis of right arm; the next day dying.		+
C. r. 209	Intestine.	5	1	Paretic in the arms, back crooked.		+

Number and Species.	Source of injected material.	Period of incubation.	Duration.	S y m p t o m s .	Anatomical changes.	
					Infil- tration.	Degene- ration.
C. B. 223	Spinal cord fr. No. 209.	3	< 1	Found dead.		+
C. B. 208	Mouth.	1	2	Lying on bottom of the cage, paretic in all the extremities; strabismus convergens.		+
C. f. 221	Spinal cord fr. No. 208.	19	1	Paralytic in the legs, paretic in the arms.		+
C. s. 201	Intestine.	5	< 1	Found dead.		+
C. f. 222	Spinal cord fr. No. 201.	(36)	1	Thin, general debility; in the afternoon, paretic in the legs, especially the right one; patellar reflexes absent on right, weak on left side.		+
C. B. 170	Intestine.	13	< 1	Found dead.		+
M. r. 191	Spinal cord fr. No. 107.	(47)	< 1	Sitting on the bottom of the cage, does not like to move; died in the evening.		+
M. r. 164	Mouth.	8	18	Weak, climbs badly; 14:th day, paretic in the left leg; 18:th day paretic in all extremities.		+
C. f. 177	Mouth.	10	< 1	Found dead.		+
M. r. 188	Intestine.	7	1	Paresis of the legs; in the evening of the same day completely paralyzed: paretic in the arms also.		+
M. r. 283	Mouth.	16	2	Crooked back, does not climb; the patellar reflexes weak on left side.		+
M. r. 281	Mouth.	16	< 1	Found dead.		+
M. r. 282	Mouth.	20	5	Paretic in the legs; patellar reflexes reduced; 2:nd and 3:rd day, increasing muscular weakness. 5:th day, dying.		+

Table VI.

Monkeys infected with secretions from convalescents after infantile paralysis.

Number and Species.	Source of injected material.	Period of incubation.	Duration.	Symptoms.	Anatomical changes.	
					Infiltration.	Degeneration.
M. c. 95	Mouth.	2	5	Paretic in the legs; 3rd day also in right arm; 4th day, in both arms.	(+)	+
M. c. 94	Intestine.	16	4	Paretic in the legs; found dead after 4 days.		+
M. r. 127	Mouth.	16	19	Climbs with jerks (paretic in the arms?). Increasing paresis of arms and legs from the 14th day onwards.		+
M. r. 123	Intestine.	20	1	Paretic in arms and legs; lying on the bottom of the cage in the evening of the same day.		+
M. r. 149	Mouth.	4	7	Weak, limping, does not climb; 6th day, distinct paresis in left arm.		+
M. r. 265	Mouth.	(49)	1	Sitting on bottom of cage; does not like to walk or climb.		+
M. f. 162	Mouth.	20	4	Debility, increasing during the following days.		+
C. f. 216	Spinal cord fr. No. 162.	(50)	< 1	Found dead.		+
M. r. 163	Intestine.	(127)	1	Paretic in the legs; died the following day.	+	+
C. f. 234	Mouth.	8	< 1	Found dead.		+
M. r. 239	Intestine.	8	< 1	Found dead.		+
M. r. 98	Mouth.	2	2	Weak, slow in movements.		+
M. c. 244	Intestine.	7	< 1	Weak, climbs badly; found dead following the day.		+



Number and Species.	Source of injected material.	Period of incubation.	Duration.	S y m p t o m s .	Anatomical changes.	
					Infil- tration.	Degene- ration.
M. r. 108	Mouth.	11	5	Paretic in both arms, during the following days increasing debility.		+
M. r. 105	Intestine.	(88)	< 1	Found dead.		+
M. f. 250	Mouth.	13	< 1	Found dead.		+
M. r. 122	Mouth.	6	10	Climbs with jerks, 2nd day, paretic in left foot; 10th day, increasing general muscular weakness.		+
M. r. 121	Intestine.	9	2	Uncertain in its movements; the feet slipping when the animal jumps (paretic in the legs?). 2nd day, lying on the bottom of the cage, paretic in all the extremities.		+
M. r. 153	Intestine.	7	2	Paretic in the arms.		+
M. f. 227	Mouth.	4	3	Convulsions, paretic in left leg; 2nd day, ataxic; patellar reflexes weak.		+
M. r. 155	Mouth.	5	1	Paretic in the legs; in the afternoon of the same day, completely paralytic, weak also in the arms.		+
M. r. 120	Intestine.	17	6	General debility, weak in left leg; 2nd day, paretic in all the extremities.		+
C. s. 248	Intestine.	7	6	Paretic in both legs; 6th day, weak also in the arms. Patellar reflexes reduced.		+

If we now pass on to the study of our own material in this respect and cast a glance at the tables, we shall find rather varying figures. In order to survey them easily they have been brought together in different groups and the averages worked out (Table VII).

Table VII.

Period of incubation in days	Infections material obtained from		
	Typical cases	Abortive cases and healthy individuals	Convalescents
1	—	1	—
2—5	23	11	5
6—15	24	9	9
16—30	11	10	5
<30	4	4	4
Average:	9.4 (12.2)	9.9 (14)	9.5 (21.5)
Totals:	62	35	23

Of the monkeys infected with material from typical cases of infantile paralysis 23 have had a period of incubation varying between 2—5 days, 24 between 6—15 days. The great majority of this group have thus fallen ill after a period varying from 2 to 15 days. Amongst these, three have had such a short period of incubation as 2 days, and 9 as 3 days. 11 animals were not taken ill until after 16—30 days and 4 even show figures exceeding 30 days. One of these latter monkeys was found dead after 70 days without previously having shown any noticeable change. It may be asked whether the period of incubation was really so long as appears from these high figures. We have here, perhaps, to deal with relapses, the first outbreak of the disease, occurring at the end of the ordinary period, having been so slight, that it escaped observation. That relapses may occur will later be demonstrated by examples. In order to obtain a more exact average figure the four animals with periods of incubation exceeding 30 days have been excluded, the *average* then being 9.4. If they are included, we get an average of 12.5 (given in brackets in the above table).

Of the 35 animals infected with the buccal or intestinal secretions from abortive cases and healthy individuals, one developed symptoms of the disease within 24 hours. The microscopic examination of its spinal cord and the infectivity of the latter on inoculation into another animal proved that this monkey had really been attacked by poliomyelitis. 11 of them showed pareses after 2—5 days, 9 after 6—15 days and 10 after 16—30 days. In this group also we find 4 animals with an apparently long period of incubation, exceeding 30 days (36, 43, 47 and 59 resp.). The same principle of calculation being used as before, the *average* mean for these monkeys will be 9,9 (14) days, thus closely corresponding to the former group, where the infection had been induced with material from typical cases of infantile paralysis. This paralellism in the periods of incubation may in a way seem rather surprising, as the micro-organism contained in the secretions from the abortive cases and healthy individuals in all probability was less virulent than that in the secretions from the typical case. That this difference in virulence exists may be concluded from the anatomical changes produced. Further details on this point will be given in the next chapter.

Almost the same periods of incubation are found in the last group also, comprising 23 animals infected with secretions from convalescents, 5 being attacked after 2—5 days, 9 after 6—15 days, 5 after 16—30 days and finally four later than 30 days. In one of the last mentioned animals the disease manifested itself as late as the 127:th day after the inoculation but then took a very speedy course, the monkey dying the following day. The medulla oblongata showed distinct perivascular infiltrations and the ganglion cells of the spinal

cord were highly degenerated; thus the animal had died of poliomyelitis. It is difficult to conceive why the virus should need such a long time to reach the central nervous system from the seat of injection. We find it more easy to believe that the attack causing death was a relapse, a fresh flaring up of virus lying latent somewhere in the spinal cord or brain, and which at the first attack had not been able to cause changes sufficiently great to be clinically observed. We have previously tried to show that a spontaneous infection can hardly come into question. The *average* for the period of incubation in this group is 9,5 (21,5). The lower, more exact figure lies consequently very close to those obtained in the two preceding groups.

Our mean figures (9.4, 9.9 and 9.5) thus show a close similarity with that obtained by Römer (9.5). It is, however, remarkably that comparatively many of our monkeys have had a rather short period of incubation, in one case not more than 24 hours. The limit in the upward direction is difficult to fix; we have put it at 30 days, and regarded those beyond that figure as probably relapses.

*Symptomatology.* In our animals, as in those of other investigations, prodromal symptoms have sometimes been observed. We have had the opportunity of seeing that the monkeys a few hours before the appearance of the pareses have been less lively than before; they prefer to sit still or they climb remarkably slowly. They are often abnormally frightened and anxious, trying to hide themselves. Fine tremblings and shakings all over the body are observed in some; the appetite generally less good. These symptoms are, however, not very characteristic and the animals have often been found paralyzed without having



previously manifested anything abnormal. The temperature has not been taken.

In order to get a clearer view of the symptoms observed in our monkeys they have been arranged in different groups, partly in conformity with the manner of designation used by LANDSTEINER and LEVADITI (Table VIII). According as the paralysis has commenced in the arms or the legs they have been put under the heading of an «upper» or «lower» type, if the paralysis commenced simultaneously in the upper and lower extremities they have been classified as a «mixed type». The table further contains a statement with regard to the presence of symptoms from the brain and the cranial nerves. There is, also, a group called *general muscular weakness* and, finally, there is a column showing the number of animals found dead without having previously presented any obvious symptoms.

Of the 65 monkeys infected with material from typical cases of infantile paralysis 22, or 35.4 %, have manifested paralyse first in one or both arms, in 20 cases, or 32.2 %, the paralyse have commenced in the legs and in 5, or 8.06 %, pareses or paralyse have appeared simultaneously in the upper and lower extremities. In a comparatively large number of the animals the paralyse have consequently first appeared in the upper extremities, notwithstanding the fact that the inoculation, in the majority of cases, has been made both intraperitoneally and intraneurally into one sciatic nerve. Consequently we cannot agree with the statement made by LEINER and V. WIESNER, that the paralyse after the intraperitoneal inoculation often, if not constantly, first make their appearance in the hind part of the body. Their intraperitoneal and combined injec-

tions are, however, comparatively few as compared with their intracerebral and intraneural inoculations. 8 of our animals, or 12.7 %. have shown a general muscular weakness without any signs of a distinct paresis or paralysis located to any special part of the body. These animals are very slow and uncertain in their movements, slip easily on jumping, climb with difficulty and are easy to catch. Sometimes they have become perceptibly thin. In some of them we have also observed a reduction or loss of the patellar reflexes. The monkeys showing the symptoms now described evidently correspond to the types observed by LEINER and v. WIESNER and called by them »marasmic». The expression appears to us less happy as the symptoms are evidently due to widespread degenerative changes in the motor cells, as will be shown in the next chapter. The symptoms are thus to be considered as

Table VIII.

Source of infectious material.	Upper type.	Lower type.	Mixed type.	Cerebral and bulbar symptoms.	General muscular weakness.	Number found dead.
Typical cases of infantile paralysis.	22=35.4 %	20=32.2 %	5=8.06 %	No. 93, Commencing cerebrally, then descending = 1.6 %. No. 27, Mixed type + bulbar symptoms No. 85, Landry's type + pontine symptoms.	8=12.7 %	6=9.6
Abortive cases and healthy individuals.	6=17.1 %	8=22.8 %	4=11.4 %	No. 208, Landry's type + pontine symptoms.	10=28.5 %	7=20
Convalescents.	2=8.6 %	7=30.4 %	1=4.3 %	No. 227, Convulsions, ataxia + spinal symptoms.	8=34.7 %	5=21

real pareses, which, even if not so far advanced, are on the other hand so much more extensive. On this account we have employed the expression *general muscular weakness*.

In only one of the 62 monkeys did the illness commence with cerebral symptoms (no. 93, a detailed history of the disease being found on page 70). During the first day the monkey had repeated attacks of general convulsions lasting for a minute or two. After the attacks it rushed about, running hither and thither without any control, manifesting distinct signs of a high degree of ataxia. No paralyses could on this day be observed. Later on signs of a left-sided oculo-motor paresis manifested themselves and on the third day some spinal symptoms appeared. We have also had occasion to observe convulsions in another animal not included in the table in question. A Baboon, 13 days after an intravenous inoculation with passage-virus, was for several days repeatedly attacked with tonic spasms of the arms and legs and of the muscles of the neck and face. The animal afterwards recovered and shows at present no pareses. In two others of the monkeys in question some bulbar and pontine symptoms appeared towards the end of the illness, in one case a facial and oculo-motor paresis (no. 27), in the other a right-sided ptosis (no. 85). The paralyses commenced in both animals in the spinal cord, and then spread upwards, thus corresponding to LANDRY's paralysis.

If the clinical symptoms observed in the two remaining groups, i. e. the monkeys inoculated with secretions from abortive cases, healthy individuals, and convalescents, are examined, it is striking to notice how great the number of cases is in which no limited paralyses have been observed, but instead only a gene-

ral muscular weakness, making in the former group 28.5 % of the total number 35 and in the latter group even 34.7 % out of 23 monkeys, while only 12.7 % of the monkeys employed for the investigation of the typical cases of infantile paralysis presented the same symptom. Possibly this difference may be associated with the fact that the virus inoculated in the first group possessed a degree of virulence differing from that of the two latter groups. Besides these animals with general muscular weakness a good many are found where distinct paralyses of the extremities have been observed. But it is to be noticed that the motor changes have, as a rule, not advanced so far as to become complete flaccid paralyses but have had rather the character of pareses. In the first group, on the other hand, complete paralyses are to be found more often. We will endeavour to explain this in the next chapter. A comparatively large number of these monkeys have died without having previously shown any obvious symptoms. That they are more numerous in these groups may possibly be due to an accident. Symptoms from the brain and the cranial nerves have in these only been observed exceptionally. Thus the monkey no. 208, which was attacked with spinal symptoms presented towards the end an oculo-motor paresis, and no. 227 showed, besides signs of a spinal affection, also convulsions and ataxia.

Just as in the case of man, *relapses* of the disease have been observed in monkeys attacked by experimental poliomyelitis (LANDSTEINER and LEVADITI, RÖMER). A similar course of the disease has not so seldom been observed also by us in our experimentally injected animals. At the lapse of a longer or shorter period of time after a comparatively slight attack some



of our monkeys have been seized by a new attack, usually more severe and terminating fatally. (Vide nos. 11, 18, 50, 100, 115, 135, 136, 179). We wish to emphasize once more that those animals which became ill after a seemingly unusually long period of incubation in all probability had had a slight and unobserved attack previously. The clinical observations agree very well with the observations made by LEINER and V. WIESNER. They were able to demonstrate the presence of virulent virus in the spinal cord of a monkey as long as 24 days after the inoculation or on the 17:th day after the onset of the disease.

*The duration, prognosis and mortality of the disease.* Poliomyelitis in monkeys often takes a very speedy course. Not seldom we have found the animals dying within a few hours of the onset of the first pareses. Of the 120 animals included in the tables IV—VI 44, i. e. 36.6 %, died within the first 24 hours, in nearly one-half (45.8 %) the disease did, however, last longer, varying between 2—9 days and in the remaining 17 (14.1 %) the course has been more or less protracted.

The *prognosis* of experimental poliomyelitis in monkeys is, according to our experience, very unfavourable and this coincides with that of other investigators. Of 120 animals only 4, i. e. 3.4 %, escaped with life, while in all the others, i. e. 96.6 %, *the disease had a fatal termination*. Only in exceptional cases have we seen the paralyses disappear. The figure of mortality is thus, judging from our material, still higher than hitherto stated. According to FLEXNER and LEWIS it is 75 %. RÖMER found the disease ending fatally in 76.4 %; 6 % survived with persistent paralyses, and 17.6 % recovered completely.

As will be evident from the above description,

our animals have often presented the paralyzes characteristic of poliomyelitis, flaccid paralyzes as well as pareses, but we have not seldom found the disease manifesting itself in general muscular weakness without any distinct, limited paralyzes. In these cases the clinical picture alone is obviously not sufficient to establish the diagnosis; the histological examination and eventually also the control-inoculation must decide. But even when pareses are present poliomyelitis can not with certainty be assumed. A few examples will illustrate this. A non-inoculated *Macacus cynomolgus* which since Dec. 19 had been living in a separate cage together with healthy monkeys showed, on Jan. 9, a marked weakness of both hands; the animal was unable to grasp firmly, but otherwise was bright and lively. During the following days the weakness of the right hand and right arm increased; on jumping the animal constantly fell over to the right. During the whole time the hand was kept in the position of radial pareses. It died on Jan. 16. The spinal cord showed no distinct changes. Another *Macacus cynomolgus* which also had not been inoculated and which had been living in the same cage with the previous monkey died after having been less lively for some days and having manifested a marked weakness of one arm and hand. In this case also the histological examination showed nothing distinctive of poliomyelitis.

For our experiments we have employed various species of monkeys, but mostly *Macacus cynomolgus* and rhesus. We have used also other kinds of *Macaci*, such as *pileatus* and *sinicus*, further *Cercopithecus fuliginosus* and *Cynocephalus hamadryas*, and occasionally a *Cercopithecus Burnetti*, a *Cercopithecus sa-*

baeus or *C. ruber*. All these species have proved susceptible to an infection with poliomyelitis. As the animals have chiefly been employed for diagnostic purposes it is impossible on the basis of our material to draw any definite conclusions with regard to their varying susceptibility to the virus of poliomyelitis. Judging from the number of animals that have proved resistive to the infection, it appears to us as if *Macacus cynomolgus* were very susceptible, and *Macacus rhesus* somewhat less so. The Baboons, on the other hand, are, according to our opinion, considerably less sensitive than those first mentioned. With regard to the other species our experience is too small to allow us to draw any conclusion.

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## V. The histological changes in the spinal cord of monkeys affected by poliomyelitis.

By

*Carl Kling, Alfred Pettersson and Wilhelm Wernstedt.*

The object of our investigation being to attempt to solve a purely epidemiological question, no further histological studies were from the beginning included in our program than would be necessary to settle the diagnosis. To this end, however, a rather thorough microscopical examination proved often necessary and as the numerous positive results led to the gradual accumulation of a rich material, we have considered it appropriate to enter somewhat more closely into the question of the changes found in the spinal cords of monkeys attacked by poliomyelitis. There has been all the more reason for this as our material differs from that of previous investigators in this respect that only a very small proportion of it has been obtained by using passage-virus.

The more characteristic changes in the spinal cord of man in poliomyelitis consist, as is well known, of an infiltration of the pia with chiefly mononuclear cells, infiltrations in the spinal cord both perivascular and diffuse as well as in groups in the grey matter, degeneration of the nerve cells and im-

migration into them of mononuclear and polymorphonuclear leucocytes (leucocyte-neuronophagia). A similar picture is often presented by the spinal cord of the monkey in connection with experimental poliomyelitis. In our investigations, we have met numerous examples of this (Fig. 1). It is quite evident that it is the inflammatory cellular infiltration with leucocytes which is the most obvious change, the degeneration of the nerve cells being at times quite considerable or almost absent. Changes of the former kind may therefore be suitably called *infiltrative*.

But it is by no means always that the spinal cord of monkeys which have died of poliomyelitis present the appearances described. Often the *cellular infiltration* is entirely *absent* or, at the most, an increase with regard to the number of white corpuscles is observed in the vessels. The most striking change is instead the *degeneration of the nerve cells* in the spinal cord. The slightest degree of this degeneration is recognized thereby, that the ganglion cells are, so to say, too small for the spaces which they occupy in addition to which the tigroid substance is less distinctly marked and the cell more deeply stained than ordinarily. If the degeneration be more advanced the cells are greatly shrunken, almost entirely homogeneous, intensely stained and generally more or less intensely vacuolated or fenestrated. The vacuoles may be few and rather large or small and numerous. Through the process of shrinking and vacuolation the ganglion cells often become reduced to small, dark, irregularly star-shaped bodies or sponge-like masses. Into the nerve cells which have been changed in this manner cells belonging to the surrounding glia have often eaten their way more or less deeply. In other cases the degene-

ration of the nerve cells manifests itself in that they are slightly stained, not shrunken, the protoplasm being very finely granular or almost homogeneous and, at least at the edges, as if liquified. These cells seldom contain any vacuoles. As a rule the nuclei are also changed, sometimes deeply, sometimes slightly, but always diffusely stained, and sometimes they are broken up or entirely dissolved.

In addition to the alteration in the nerve cells, the *cells of the glia* often show distinct *changes*. They are swollen, clear and transparent and always attract the attention in that on slight magnification they appear as light spots in the grey matter. No cell-processes can be discerned, at least in preparations stained with iron-haematoxylin. After hardening in alcohol the protoplasm has a very homogeneous appearance, showing at the utmost a slight net-like marking. On freezing-sections of material hardened in formalin the cell-protoplasm has distinctly a finely granular appearance. The nucleus is often rather rich in chromatin and shows a neat chromatin-network. Sometimes nearly all the supporting cells of the grey matter appear changed in this manner, and this fact plainly indicates that it is the glia cells which have undergone this change, since no actual new formation of cells has taken place. Whether the cells of the spinal cord of a mesenchymal nature have also been changed in this manner has not been possible to decide. We have, it is true, sometimes observed rather a large number of cells of this appearance around the vessels of the cord (Fig. 5), but on the other hand they have never been found in the pia mater. Other authors do not seem to have often observed similar changes in the glia cells. SCHMAUS mentions a glia-cell-hypertrophy in

man, but it seems doubtful whether the changes observed by him have been similar to those now described by us. SCHMAUS emphasizes that the cellular processes were distinctly marked, an observation which we have never made. We have called this change in the cells of the neuroglia *hypertrophy*, a term which is not quite exact, as it is not only with regard to their size that the cells differ from the normal.

As previously mentioned, these enlarged glia cells are often found to have penetrated into the degenerated neurons. This encroachment upon the nerve cells differs in many respects from the neuronophagia hitherto generally described as found in acute poliomyelitis in man and experimental poliomyelitis in monkeys. In the latter variety the ganglion cells are encroached upon by a large number of cells, as was established by RISSLER, who was the first to observe neuronophagia in acute poliomyelitis in man. These cells, which have been studied especially by FORSSNER and SJÖVALL and by WICKMAN, are polymorpho-nuclear leucocytes and polyblasts (WICKMAN), the polyblasts, according to WICKMAN, being the real neuronophages. Both kinds of cells found in this neuronophagia-type have this in common that their protoplasm differs only slightly, if at all, from that of the ganglion cell as long as the latter is not highly disintegrated. Of the individual cells often only the nuclei can with certainty be distinguished (Fig. 4). The neuronophagia observed by us in the monkeys infected with the irrigation fluids, especially when these fluids were obtained from abortive cases and virus-carriers, have quite a different appearance from the former type (Fig. 3 and 6). In this the cells that eat their way into the ganglion cell have a large, clear, rounded cell body, sharply distinguished from



the dark protoplasm of the nerve cell, a difference which remains as long as there is anything left of the nerve cell. Some times the remnant of the neuron is found sitting like a dark hood on the large neuronophage. In other, more advanced cases the neuronophages remind one of osteoclasts eating their way into bone. The boundary between neighbouring neuronophages is often rather difficult to find, the appearance at times resembling that of a giant cell, but we have never observed any karyokinetic figures in them (Fig. 7). The destruction of the nerve cells by these glia cells evidently takes place in a manner differing from that caused by the polyblasts. In reality it seems very doubtful whether this kind of neuronophages, if this term can be applied to them at all, take up the ganglion cells or their remnants as formed bodies. We have never been able to detect, at least in Marchi-preparations, any great number of fat-granules in them. These neuronophages are evidently only enlarged glia cells surrounding the ganglion cell. We have called this process *glia-cell-neuronophagia* and grouped together the changes of the nervous system characterized in the above description under the term of *degenerative*.

In some cases the two types of changes have been found together, the spinal cord showing both cellular infiltration, commonly surrounding the vessels, and degeneration of the nerve cells, neuroglia-neuronophagia and enlargement of the neuroglia cells, but no leucocyte-neuronophagia (Fig. 2).

Some points have already been stated in support of the view that changes of the kind observed by us are also due to, and to some extent characteristic of, the virus of poliomyelitis. We have cases where, after injection of the same material into different animals, changes of the two

different types were obtained. Baboon no. 93 was inoculated with spinal cord of *Macacus cynomolgus* no. 72, and 19 days later *Cercopithecus Burnetti* no. 140 was injected with material from the same specimen. The former exhibited infiltrative, the latter showed degenerative changes in the spinal cord. LEINER and v. WIESNER have probably had similar changes in some of their so called »marasmic» types.

Of very great interest is the proportion between the cases in which infiltrative and degenerative changes have been observed in the experimental animals from the three different groups: typical cases, abortive cases and virus-carriers, and convalescents. Out of 59 dead monkeys belonging to the first group 25 (= 42 %) showed infiltrative, and 34 (= 58 %) degenerative changes; of the 34 monkeys belonging to the second group one (= 3 %) infiltrative, and 33 (= 97 %) degenerative; and of the 23 animals of the third group 2 (= 8 %) infiltrative and 21 (= 91 %) degenerative changes. Of the monkeys inoculated with the spinal cords of patients who had died of poliomyelitis 8 died and of these 2 showed infiltrative and 6 degenerative changes.

What is the reason that the changes observed after an inoculation with irrigation fluids from abortive cases and virus-carriers have less often been of the infiltrative variety than those produced by the specimens from typical cases of poliomyelitis, i. e. comparatively severe cases? In order to explain this point we must draw attention to the well known fact that certain organisms show a parallelism between their virulence and their power of producing an inflammatory effect. In the case of the tubercle bacillus, for instance, its power of producing exsudations is diminished at the

same time as its virulence decreases, its capacity of producing new formed tissue being still retained. Further, let us call attention to some observations with regard to the virus of infantile paralysis. LANDSTEINER and LEVADITI have pointed out that the cellular infiltration is often more marked in monkeys inoculated with passage-virus, a fact which we also have been able to verify. We have previously pointed out that cellular infiltration has sometimes not been observed in the spinal cords of monkeys inoculated with specimens from typical cases of infantile paralysis (Fig. 3). The control animals inoculated with these spinal cords have, on the other hand, shown considerable infiltrations (Fig. 4). In successful inoculations into rabbits with the virus of infantile paralysis no cellular infiltrations are obtained but only degenerative changes in the ganglion cells of the spinal cord. The virulence of the microbe is increased by passage, passage-virus being generally more effective than the original virus. *The greater virulence and the appearance of the inflammatory infiltration evidently go hand in hand in the monkey.* It is further obvious that the rabbit has greater power of resistance against this microbe than the monkey, or, in other words, the microbe is less virulent to the former animal. This is perhaps the reason why the rabbit does not show any cellular infiltration in its spinal cord. We have further seen that only degeneration of the ganglion cells and neuronophagia of the type caused by small numbers of great, clear cells, but no cellular infiltration, have been produced by specimens obtained from convalescents, whereas the specimens obtained several months previously from the same individuals during the acute stage of the disease, have produced experimental poliomyelitis characterized by consider-

able cellular infiltration. It is a well known fact that some organisms which remain on the mucous membranes a long time, e. g. the bacillus of diphtheria, often become less virulent. In all probability the same thing applies to the organism of infantile paralysis. We have thus reason to believe *that the absence of more considerable exsudations in the spinal cords of the infected animals indicates a change, and more especially a weakening of the virus of infantile paralysis*, a supposition which well agrees with the circumstance that those specimens which have produced changes of this kind have been obtained as a rule from persons who have been either only slightly or not at all ill.

Many of the monkeys infected with material from typical cases during the acute stage of the disease and the majority of those inoculated with secretions from abortive cases, virus-carriers and convalescents have shown degenerative changes in their spinal cords without having presented any isolated flaccid paralyses during life, but only pareses and muscular weakness. This clinical manifestation seems to correspond very well with the changes found to exist in the ganglion cells. A slight degeneration of the cells of the anterior horns as well as a slight encroachment upon them by the glia cells ought not to completely abolish their functions; naturally rather advanced changes are required for this and these presumably first appear during the very last stage of illness. If the degenerative change in the nerve cells be evenly distributed over the entire spinal cord as, in fact, has often been observed in our cases, the predominating clinical picture ought to be a progressive general muscular weakness without any isolated paralyses rather than the form in which definite local para-



lyses coexist side by side with muscles showing good motor power.

As the exudative infiltrations can often be entirely absent it is obvious that the degenerative changes in the nerve cells now in question must be regarded as directly due to the virus of infantile paralysis and not to trophic disturbances caused by the infiltration. Our observations contradict the view that the products of degeneration of the ganglion cells give rise to the inflammation, since a wide-spread degeneration of these cells has been very often observed without any perceptible exudation. It cannot rightly be argued that the exudations have perhaps not had time to develop on account of the speedy course of the disease, since this has sometimes lasted for several days. Although we have found these degenerations to be the commonest and most prominent changes in the spinal cord of those monkeys now under discussion, on the other hand, we do not believe, as LEINER and V. WIESNER, that the degeneration always precedes the inflammatory exudation nor that it is the cause of this. In man rather a considerable degree of cellular infiltration is at times observed, both perivascular, diffuse and in groups in the grey matter, the ganglion cells all the while only showing slight changes. Such observations have been made by WICKMAN, especially with regard to the bulbar nuclei, by HARBITZ and SCHEEL and others. We have lately observed a similar case ourselves, also a bulbar form; this is recorded on page 228, where also a short description is given of the microscopic changes in the cervical cord. Only slight changes were found in the ganglion cells, whereas a rather intense, diffuse, group-like and perivascular cellular infiltration was present. RÖMER has made similar observations in

monkeys. In our experiments, it is true, we have not observed such a change due to the effect of the virus that there was caused only infiltrative changes without degeneration of the ganglion cells, but we have observed a considerable increase of the inflammatory exudation already after one single passage. *According to our opinion the degeneration of the ganglion cells as well as the cellular or humoral exudation are to be regarded as the result of a direct injurious influence of the virus.* At times the inflammatory irritation predominates while the degenerative effect is less marked. Sometimes the virus is perhaps too weak to produce distinct exudation but sufficiently effective to produce a degeneration of the nerve cells and a progressive disturbance in the nutrition and a resulting enlargement of the neuroglia cells.

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VI. Histological examination of those mucous membranes which, on account of the presence of the micro-organism of Infantile Paralysis, may be suspected to be the point of entrance of the virus.

By

*Carl Kling and Alfred Pettersson.*

Our previous investigations have shown that the existence of the virus in the mouth, pharynx, trachea and intestine can be demonstrated so often, that it is justifiable to regard the micro-organism as being constantly present in these places in persons suffering from the disease. The presence of the micro-organism of infantile paralysis in the same parts of the bodies of perfectly healthy persons living in the surroundings of those attacked seems to point to the fact, that it has probably come from outside. The existence of the microbe on the mucous membranes and successful inoculations of monkeys through these membranes make it probable that these are the real seats of entrance of the virus. Under such conditions, and since experiments on animals have shown that the virus also can leave the body by way of the mucous membranes, the question arises whether any histological changes in the membranes are to be found as traces of

the passage of the virus. At the autopsies a swelling of the solitary follicles and Peyer's patches of the intestine and an enlargement of the mesenteric glands are constantly noticed. Clinically a redness and even a catarrhal inflammation of the pharynx and the upper respiratory passages is often observed and at times also swelling of the tonsils and the cervical lymphatic glands. On this account we have deemed it worth while to subject the mucous membranes in question to a microscopical examination, all the more as such examinations have previously only been made on a very small scale, a fact that is easy to explain when it is borne in mind that all the interest has been concentrated on the nervous system, where judging from the clinical symptoms greater changes could *à priori* be expected. With regard to the nose and mouth, we have restricted our investigations to the tonsils, in which we expected to find the greatest changes.

In his report on the epidemic in New York of 1907 STRAUSS states that he has observed enlargement of the thymus, swelling of the mesenteric glands and of the patches of Peyer, and distinctly marked Malpighian bodies in the spleen. The microscopic examination had revealed hypertrophy of the lymph-follicles and «acute inflammation» of the spleen and the mesenteric glands.

V. WIESNER found the pathological changes of the internal organs rather inconsiderable in cases of infantile paralysis. With regard to the hyperplasia of the lymphatic tissue, which he also has observed, he scarcely believes this to be due to the virus of infantile paralysis, but has called into question whether persons with a lymphatic constitution are not more liable to be attacked and more easily succumb to the disease.

LANDSTEINER and LEVADITI examined the tonsils of a 2 years' old boy, and succeeded in infecting a monkey with poliomyelitis. The illness had commenced as a lacunar angina. On the mucous membranes they found commencing ulcerations in different places, the epithelium being crowded with migratory cells, the latter also



being found in the exudation which covered the mucous membrane in some places.

FLEXNER, PEABODY and DRAPER studied the changes of the internal organs in general in 11 cases of infantile paralysis. In two cases they found distinct changes consisting in degeneration of the parenchymatous organs and a general hypertrophy of the lymphoid tissue. The latter consisted chiefly of a hyperplasia of the cells in the proliferating centra and lymph-sinuses of the lymphatic glands.

The changes in the nasal mucous membrane of monkeys, infected with poliomyelitis by simply painting them with some virus-containing material, have been examined by LEVADITI and DANULESCO. They found the epithelial layer infiltrated by polymorphonuclear and the submucous tissue by mononuclear leucocytes.

Our investigation includes five cases, all of which have had a rather speedy course. Four have been nursed at the Epidemic Hospital of Gothenburg and one in Stockholm. The organs have first been hardened in formalin and then in alcohol.

### I. *Vera Elsa Ch. B*—g, 20 years of age.

She had for two weeks prior to the onset of the illness been staying in Gothenburg where she had lived in a part of the town in which up to that time no case of infantile paralysis had occurred. Before that she had been in Stockholm. She was taken ill, on May 26, with fever and headache. On May 27, she was better and performed her usual work. On May 28, worse, suffered from an intense aching pain in the back, but not in the neck, nor in the legs. On May 30, the pains in the back were intense, in the evening weakness of the legs, especially the left, occurred which finally made it impossible for her to stand.

She was admitted, on May 31, to the Epidemic Hospital of Gothenburg. The colour of the face pale and cyanotic, stiffness of the neck but no pain, some difficulty in speaking and swallowing, the arms flaccid and almost completely paralyzed, flaccid paralysis of the left and marked paresis of the right leg, the abdomen flaccid, respiration only abdominal. The reflexes of the lower extremities and of the abdomen absent. The sensibility normal. She died in the afternoon.

At the autopsy, on June 6, the tonsils, submaxillary salivary

glands, pieces of the trachea, main bronchi and of the intestine and some of the mesenteric glands were preserved.

The *tonsils* not distinctly enlarged. The epithelium on the surface of a normal appearance, but in the crypts it is succulent and partly desquamated, invaded by a small number of leucocytes, chiefly mononuclear, but also polynuclear. The blood vessels are fairly distended and some are rather rich in leucocytes of chiefly mononuclear type.

In the *submaxillary gland* the interstitial tissue around the ducts is rather extensively infiltrated by round-cells provided with a very small cell body and a rounded or somewhat irregular nucleus, containing a large quantity of chromatin-substance. The glandular epithelium of normal appearance.

The *trachea* and *bronchi*. The outer layers of the epithelium are here and there desquamated and imbedded in the mucus covering the mucous membrane, the secretion containing a fair number of cells, both desquamated epithelium and mononuclear leucocytes. The columnar cells of the epithelium are often swollen, bottle-shaped, clear and transparent; here and there mononuclear leucocytes are noticed in the epithelial layer. The vessels of both the mucosa and submucosa are greatly distended. In some places of the mucous membrane, and also in the submucous tissue, irregular, rounded or elongated groups of cells are observed, the latter being provided with a usually rounded, sometimes oval or kidney-shaped nucleus, rich in chromatin and a small, slightly stained cell body (Fig. 10). The groups are sometimes lying closely beneath membrana propria, sometimes they infiltrate or surround the glandular lobules or their efferent ducts, similar cellular infiltrations being also found in the peribronchial tissue.

In the *intestine* the patches of Peyer and especially the solitary follicles a good deal swollen. The mucous membrane does not admit of any closer examination on account of post-mortem changes. In the submucous tissue the swollen lymphatic apparatus seems to consist of lymphatic cells of ordinary appearance. No cellular infiltration either in the muscular or subserous layer.

The *mesenteric glands* are only very slightly swollen and otherwise show no distinct change.

## II. *Knut O—n*, 4 years of age, from Gothenburg.

The boy was admitted to the Epidemic Hospital of Gothenburg in the evening of June 15, 1912, on account of symptoms of croup.

He did not suffer from croup but from a marked respiratory paresis, the inspiration being superficial and accompanied by a contraction of the cervical muscles. The legs were flaccid, completely paralysed and without reflexes, the arms very paretic. He died on June 16. Post-mortem examination the same day.

The *tonsils* not perceptibly enlarged but intensely hyperaemic. The epithelium is on the surface perfectly well preserved and of a normal appearance, but in the crypts it is succulent and invaded by mononuclear leucocytes. In some crypts plugs are seen containing rather numerous mono-nuclear and polymorpho-nuclear leucocytes. In some of the vessels are seen many white blood corpuscles.

In the *submaxillary gland*, scattered in the interstitial tissue, especially around the efferent ducts, small areas of cells are seen, showing a dark nucleus rich in chromatin and a small cell body, in appearance resembling lymphocytes (Fig. 9). The epithelium is of normal appearance.

The *trachea* and larger *bronchi*. The epithelium generally preserved, only here and there a slight desquamation noticeable. Some of the columnar cells are bottle-shaped, swollen, clear, and transparent. The lumen contains only a small quantity of mucus in which desquamated epithelium and a few round-cells are to be found. The vessels are not more filled than normally, no leucocytosis, a slight degree of cellular infiltration in the mucosa and submucosa.

The *intestine*. The mucous membrane generally rather rich in cells, the lymphatic follicles swollen and their surroundings infiltrated by similar cells, especially in the submucous tissue, where they are collected into long, transverse lines. Also between the two muscular layers or more seldom in them, some small accumulations of cells are observed in the lymph-spaces, the cells being of the same appearance as in the mucosa and submucosa.

The *mesenteric glands* are hyperaemic and the sinuses full of mostly small cells provided with a rounded nucleus rich in chromatin and with a body poor in protoplasm, the whole cell resembling a lymphocyte, and between these other cells with larger nuclei, poorer in chromatin and richer in protoplasm, as well as some polymorpho-nuclear leucocytes, are seen.

III. *Johan Harald A—k*, 5 years of age, from Stockholm.

The boy was taken ill, on June 10 with fever. On June 11 he was well again, but on the following day he had a sore throat and on the 13:th he experienced difficulty in speaking and when swallowing, the food was brought back.

Was admitted to the Epidemic Hospital of Stockholm on June 15. The general condition good, the two halves of the face asymmetrical, the right corner of the mouth standing lower, and the right half of the face not moving when he speaks; he can close the left eye better than the right, the movements of the eyes normal, the speech is indistinct, unarticulated but the voice not hoarse. No pareses of the arms or legs, and the reflexes of the extremities are normal. The pharynx is pale and shows no membrane. June 17, he is stiff in the neck, can only swallow liquid food, and this is partly returned. In the afternoon, drowsy, groans. In the evening a quick change for the worse, is unable to swallow the saliva which collects in the throat; he is unable to cough or to speak, is cyanotic. Died in the morning of June 18.

Autopsy the same day. Vivid hyperaemia of the pia mater of the brain, the cortex of the brain is of a dark reddish-violet colour and the substance of the brain is more moist and more congested than normally. The membranes of the spinal cord are rich in blood, on section the spinal cord swells markedly in the cervical and dorsal regions, is moist and the grey matter is reddishly discoloured, showing red dots and streaks. The mucous membrane of the pharynx is slightly reddened and the lymphatic glands of the neck swollen, hyperaemic. The mucous membrane of the trachea and the larger bronchi has also a rather vivid reddish hue. In the lower part of the ileum the patches of Peyer and solitary follicles are a good deal swollen, the mucous membrane rose-coloured, the follicles of the colon being also swollen.

On microscopic examination the *tonsils* show hyperaemia, some of the blood vessels are richer than normally in white blood-corpuscles, chiefly of a mono-nuclear type. The epithelium on the surface of normal aspect. In most of the crypts it is, on the other hand, succulent and covered by a coating consisting of a fine thread-like, fibrinous mass containing a great number of polymorpho-nuclear leucocytes and a small number of mono-nuclear cells (Fig. 8). Between the epithelial cells numerous small cells with round nuclei rich in chromatin and small-seized cell body may be observed in these places. The proliferating centra are enlarged, appearing as succu-



lent light coloured islets consisting of some larger and some smaller cells; the large cells being provided with a rounded or oval, slightly stained nucleus, the small cells with a round nucleus rich in chromatin, the cell body being small and difficult to discern.

The *submaxillary* gland. In different places in the interstitial tissue accumulations of lymphocytes are observed. In some of the groups the central cells are lying less closely, similar to the arrangement in the proliferating centra. The glandular epithelium has a normal appearance.

The *trachea* and the larger *bronchi*. The epithelium is mostly desquamated, the membrana propria being exposed, the epithelial cells being retained only in those places where the mucous membrane forms a fold. The vessels of the mucous membrane are greatly distended with blood and often remarkably rich in white blood-corpuscles. The mucous membrane is generally very rich in cells and in some places the cells form smaller or larger groups or longitudinal streaks, especially between the mucosa and the submucous tissue. In the latter similar foci are seen finding their way in between the glandular lobules. These groups consist of small, mostly mono-nuclear cells with rounded or somewhat irregular nucleus rich in chromatin and of varying size. They look like lymphocytes. In different places polymorpho-nuclear leucocytes in small numbers are observed. Also the peri-bronchial connective tissue contains similar groups of leucocytes in the lymphatic vessels and in the interstices of the connective tissue. The vessels of this part sometimes also contain numerous white corpuscles, the majority being of a mono-nuclear type. The bronchial glands are greatly hyperaemic and the sinuses quite full of cells.

The *intestine*. The mucous membrane is very rich in cells and the solitary follicles are greatly swollen. The cells are generally small, some of them having a small, irregular nucleus rich in chromatin, others are provided with a larger, paler nucleus. The central portion of the follicles sometimes consists of cells, resembling proliferating centra. On the villi the epithelium mostly desquamated, but in the glands it is well preserved. The submucous tissue is, at least in some places, rather hyperaemic and some of the vessels very rich in white blood-corpuscles. In the muscular and subserous layers no distinct cellular infiltration is seen.

The *mesenteric glands* are slightly swollen, highly hyperaemic, and the investing sinuses filled with small cells.

The *spinal cord* in the cervical region is hyperaemic and the grey matter displays rather numerous and fairly large haemorrhages. Slight cellular infiltration of the pia on the anterior surface, more marked in the anterior fissure, and of a considerable extension around all the large as well as middle sized vessels of the white and the grey matter, the grey substance showing also a considerable diffuse and group-like cellular infiltration. The glia cells are not enlarged. The majority of the ganglion cells have a comparatively normal appearance showing distinct tigroid substance and a distinctly stained nucleus; in a small number, however, the cell body is somewhat homogeneous, but no neuronophagias are found.

IV. *Gustaf S—n*, 2<sup>1</sup>/<sub>2</sub> years of age, from Gothenburg.

The boy was taken ill on June 30 with fever; he was sleepy, had no catarrhal symptoms. On July 3 weakness of the right leg was observed. The patient has six brothers and sisters, all of whom were well, but in the same house a two years' old child belonging to another family had been attacked by infantile paralysis. This latter family had, however, had no intercourse with the family to which the boy belonged.

He was admitted to the Epidemic Hospital of Gothenburg on July 5. Has fever and is very stiff in the neck; marked pareses of the right arm, less marked of the left one, almost complete paralysis of the right leg and marked paresis of the left; the breathing chiefly abdominal; patellar reflexes absent. The salivation remarkably profuse, the patient continuously expectorating. July 7, the breathing still more hampered, died the same day. Autopsy on July 8.

The *tonsils* are not enlarged and the epithelium is normal, the crypts contain old plugs of hyaline appearance and poor in cells. No distinct hyperaemia, some of the smaller vessels are filled with loose, thread-like fibrinous masses rich in leucocytes. In front of the tonsil towards the base of the tongue the epithelium is in some places succulent and desquamated, exposing the lymphoid tissue beneath. The mucous glands are here of normal appearance.

The *salivary glands* look normal, nowhere can any lymphoid tissue be observed.

The *trachea* and the larger *bronchi*. The greater part of the epithelial layer is desquamated and imbedded in the mucus, which in moderate quantities covers the mucous membrane and which in

some places contains a fair number of polymorpho-nuclear leucocytes. The remaining epithelium is succulent and invaded partly by small cells resembling lymphocytes and provided with a small round nucleus rich in chromatin, partly by larger cells showing an irregular, often kidney-shaped, slightly stained nucleus and a somewhat larger cell body, and finally by solitary polymorpho-nuclear leucocytes. Also in the membrana propria itself similar cells are sometimes observed. The mucosa is very rich in cells presenting the appearance just described, and in the submucous tissue they are arranged here and there in streaks or rounded groups. Both the mucous membrane and the submucous tissue are markedly hyperaemic.

In the *intestine* neither the solitary follicles nor the patches of Peyer are swollen and on microscopical examination no pathological changes are found present.

The *mesenterical glands* are slightly hyperaemic, some vessels are rich in white blood-corpuscles and some are filled with loose, thread-like fibrinous masses.

V. *Naemi Maria L—k*, 8 years of age, from Gothenburg.

The girl was taken ill, on July 9, with fever, headache and vomiting and was drowsy. On July 12 she was obliged to remain in bed. July 13, she complained of pain in the neck and in the afternoon the arms began to get weak.

In the evening she was admitted to the Epidemic Hospital of Gothenburg. The patient is pale and ill, no stiffness of the neck, flaccid paralysis of the cervical and dorsal muscles, is unable to lift the head from the pillow, marked paresis of the muscles around both shoulder-joints, the strength of the hands and fingers being, however, good, and she is able to move the forearms; the breathing almost entirely abdominal, paresis of the quadriceps femoris muscle on both sides, no patellar reflexes. July 14, no costal breathing, the abdominal respiration considerably reduced, marked cyanosis, severe pains in the extremities. Died in the evening. Autopsy on July 15.

The *tonsils* not enlarged, the epithelium is well preserved on the surface but at the bottom of some of the crypts it is succulent and desquamated and rather profusely invaded by mono- and polymorpho-nuclear leucocytes, a small number of similar cells being

also collected within the crypts. The proliferating centra are very distinctly marked. Otherwise the tonsils show no change excepting that the vessels are remarkably rich in mono- and polymorphonuclear leucocytes. In the neighbourhood of the tonsil proper the epithelium, on the other hand, is desquamated in places, small accumulations of lymphoid tissue lying almost exposed.

The *submaxillary gland* is moderately hyperaemic showing in different places around the efferent ducts minor accumulations of small, lymphocyte-looking cells. The glandular epithelium does not show any change.

The *trachea* and the larger *bronchi*. The epithelium is to a very great extent desquamated and imbedded in the mucus which, to a small quantity, is found in the lumen, the innermost epithelial layer is often left. The mucous membrane is on the whole not richer in cells than normally, but at different places, especially in the bronchi, moderate sized accumulations of small cells are observed resembling lymphocytes and provided with a nucleus that is rich in chromatin. These foci sometimes form small projections in the mucous membrane and sometimes they are seen also in the submucous tissue, finding their way in between the glandular tubules. The mucosa and submucosa are moderately hyperaemic but the bronchial lymphatic glands, on the contrary, markedly so.

In the *intestine* the solitary follicles are greatly swollen, with distinct proliferating centra, but otherwise no marked cellular infiltration can be observed anywhere. Both the mucous membrane and the submucous tissue are markedly hyperaemic.

The *mesenteric glands* are slightly swollen and hyperaemic.

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As was to be expected, the examination has not disclosed any great changes in the organs in question, but some minor changes have been observed and these are of such a nature that they seem worth while to be discussed.

The epithelium lining the crypts of the *tonsils* was succulent and in some places desquamated, in others invaded by lymphocyte-looking cells, the latter, as a rule, being found also in the exudation contained



in the crypts. In two cases the quantity of the exudation was greater and contained also poly-nuclear leucocytes. It is worth mentioning that in one of these cases the illness commenced with a sore throat. In four cases the blood vessels have been remarkably rich in leucocytes, the greater number of these being mono-nuclear cells. In two cases the epithelium in the neighbourhood of the tonsils was desquamated, exposing the lymphoid tissue here.

The *salivary glands* examined have in four cases shown a more or less marked infiltration with lymphocytes, especially around the efferent ducts, and in one case a certain resemblance to the proliferating centra of the follicles of lymphatic glands was observed.

The *trachea* and the *bronchi* presented in one case very slight changes, viz. desquamation of the epithelium and degeneration of some of the epithelial cells. But in the other cases a desquamative, catarrhal inflammation was seen, with marked infiltration of lymphoid cells, hyperaemia of the mucous membrane and of the submucous tissue and, in one case, distinct leucocytosis in the vessels.

The *solitary follicles* of the *intestine*, with the exception of one case, have been markedly swollen, besides which, in one case there was a distinct accumulation of lymphocytes in the lymphatic vessels of the submucous and muscular layers and finally on another occasion was observed a leucocytosis in the blood vessels.

The *mesenteric glands* were, in four cases, more or less swollen and hyperaemic.

*The most constant change, as has already been pointed out by other observers, is the great prevalence of lymphoid tissue and infiltration by lymphoid cells. It is*

naturally very difficult to decide, whether these changes really are pathological and, this being so, whether they are due to the virus of infantile paralysis. But if it be taken into consideration that this virus has a great inclination to cause infiltration of especially mono-nuclear cells and that the blood vessels are often rich in leucocytes in those places where cellular infiltration occurs, while as a rule no common leucocytosis is present in infantile paralysis, it seems more probable that the above mentioned cellular infiltrations should be due to the virus of infantile paralysis rather than, as v. WIESNER believes, lymphatic individuals from nature should be especially liable to the disease.

Besides the changes now mentioned we have in four cases found *catarrhal tracheitis and bronchitis of a special kind*, inasmuch as, with the exception of one case, only very few polymorpho-nuclear leucocytes have been observed, but, on the other hand, a not inconsiderable infiltration and exudation of mono-nuclear cells. This seems to us to argue in favour of the explanation that the inflammation in the air-passages has been due to the virus of infantile paralysis itself and not to a secondary infection. According to our opinion this circumstance supports the opinion that the lymphatic cellular infiltration and the increase in lymphatic tissue is an expression of some irritation of the organs in question caused by the microbe. The desquamation of the epithelium observed in the trachea and the bronchi, as well as around the tonsils, has probably also facilitated the infection by admitting greater quantities of the virus, provided the desquamation has occurred fairly early. With regard to human beings, who apparently have rather a great power of resistance against the disease, the quantity of virus ad-

mitted into the body is likely to be of some importance in the question of the appearance or non-appearance of the disease. Whether the inflammation of the tonsils in those cases where the crypts have contained a greater number of polynuclear leucocytes has been due to the virus of infantile paralysis or to some other micro-organism, is very difficult to decide. Should the latter be the case, it may be imagined that the tonsilitis has facilitated the entry of the virus of infantile paralysis.

If the swelling of the lymphoid apparatus of the intestine should be due to the virus of infantile paralysis, which seems to us most probable, this does, however, not justify any conclusions regarding the eventual occurrence of the infection through the invasion of the infective agent by way of the intestine. As the virus exists in the nose, mouth and pharynx, greater or smaller quantities of it are constantly being swallowed. Through the investigations of FLEXNER, CLARK and DOCHEZ it is known that it can pass through the stomach in a more or less undamaged condition. The changes in the intestine may very well be secondary to the onset of the disease and be due only to a constant irritation of the intestine caused by the swallowed virus.

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## B. Some epidemiological experiences from the great epidemic of Infantile Paralysis which occurred in Sweden in 1911.

By

*Wilh. Wernstedt.*

It has fallen to the lot of the Scandinavian Peninsula to play an important rôle in the history of epidemics of infantile paralysis. The very first known epidemics of undoubted poliomyelitis occurred here — in Norway 1868 and in Sweden 1881. When the disease made its appearance a quarter of a century later in the form of large epidemics comprising entire countries, or great parts thereof, it started a new from the Scandinavian countries. Last year a similar great epidemic of infantile paralysis visited the Northern countries and in Sweden caused a devastation, that, if consideration be taken of the number of population, probably exceeded in extent that of any hitherto known epidemic of infantile paralysis that has visited any country.

It is natural that the reappearance of such a large country-epidemic after the lapse of so many years of comparative exemption should invite to a renewed study. Besides, one cannot but think that a comparison between the two large epidemics of 1905 and 1911

must give some deeper knowledge of this disease. In the following a brief account will be given of some of the results arrived at in the studying of the second large epidemic of infantile paralysis in Sweden. A more thorough and detailed investigation of the rich material available must be reserved for a future publication.

### Previous epidemics in Sweden.

It may be of interest in the first place to call to mind, in a few words the previous epidemics of this disease in our country. In his annual report for 1881 to the Royal Board of Directors of the Medical Department, Dr. BERGENHOLZ communicated his observations on a small epidemic of 18 cases of poliomyelitis, which occurred during that year in one of the northern parts of Sweden (in the neighbourhood of Umeå). In 1887 an epidemic of infantile paralysis occurred in Stockholm (43 cases), and in 1895 another epidemic in the same city (21 cases), both of which have been studied by Prof. O. MEDIN.<sup>1</sup> Before the outbreak of this latter epidemic in Stockholm, Dr. J. LARSSON had observed, in 1888, a minor epidemic (14 cases) at Ämmeberg, in the middle part of Sweden. Dr. Larssons account is to be found in his annual report to the Royal Board of Directors of the Medical Department, but has hitherto escaped being mentioned in the literature. In 1899 infantile paralysis appeared for the third time epidemically in Stockholm (54 cases). In 1903 a small epidemic comprising 20 cases is known to have occurred

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<sup>1</sup> MEDIN, O., L'état aigu de la paralysie infantile. Arch de méd. des enfants, 1898.

in the second city of Sweden, Gothenburg (situated on the west coast).

Far more serious than all these epidemics was that which visited our country in 1905 and which has been studied by Wickman.<sup>2</sup> More than 1000 cases occurred in Sweden during that year. Almost every part of the country was affected by it and several places were to a considerable extent devastated. Since then the disease has every year made itself remembered by some smaller accumulations of cases or epidemics occurring in various parts of the country, the total number of cases observed during this period of time being comparatively great. With every successive year since 1905 the number of cases has, as will appear from Table I, generally decreased until last year when the epidemic quite unexpectedly blazed up in different parts of the country and, rapidly increasing, at length involved almost the whole land. When only those that were known to the physicians, are counted, it comprised more than 3800 cases (Table II).

### Extension and course.

The first signs of this recrudescence of a great epidemic of infantile paralysis in our country can be detected in the early spring of 1911. Already at that time we can observe epidemic accumulations in four localities in the country widely apart from each other (map 2.). Towards the end of *March* and in the beginning of *April* a small group of seven cases were observed in the parish of Färila in the county of Gäfleborg (XX) the cases occurring in different villages within a rather

<sup>2</sup> WICKMAN, J., Beiträge zur Kenntniss der Heine-Medinschen Krankheit (Poliomyelitis acuta) und verwandter Erkrankungen, Berlin 1907.

Table I.

Number of cases of Infantile Paralysis reported from the respective counties and the three largest towns of Sweden during 1905—1911.

	1905	1906	1907	1908	1909	1910	1911	1906— 1910
Stockholm's town	10 <sup>1</sup>	—	—	1	1	—	204	2
I Stockholm's county	1	4	7	7	3	1	175	22
II Upsala »	1	1	15	9	4	2	67	31
III Södermanland's »	44	3	6	3	19	5	88	36
IV Östergötland's »	101	17	4	14	9	8	178	52
V Jönköping's »	51	8	26	18	11	6	1065	69
VI Kronoberg's »	263	95	14	56	6	5	88	176
VII Kalmar »	67	29	4	3	15	1	219	52
VIII Gotland's »	—	—	—	—	4	1	14	5
IX Blekinge »	10	6	33	3	2	2	11	46
X Kristianstad's »	14	15	73	7	3	2	44	100
XI Malmöhus' »								
a) Malmö town	—	—	22	—	—	—	3	22
b) the rest of the county	5	3	68	4	9	1	102	85
XII Halland's »	1	—	10	1	3	—	27	14
XIII Göteborg's & Bohus' »								
a) Göteborg's town	—	—	15	2	—	2	30	19
b) the rest of the county	—	6	11	21	2	3	24	43
XIV Älfsborg's county	9	2	21	29	—	1	341	53
XV Skaraborg's »	136	6	21	6	5	3	114	41
XVI Värmland's »	58	16	8	36	7	10	27	77
XVII Örebro »	88	8	13	32	6	6	31	65
XVIII Västmanland's »	42	13	—	—	1	2	199	16
XIX Kopparberg's »	13	54	4	2	2	—	130	62
XX Gäfleborg's »	18	5	2	10	11	1	98	29
XXI Västernorrland's »	38	12	2	18	10	4	300	46
XXII Jämtland's »	9	16	2	14	4	89	114	125
XXIII Västerbotten's »	31	16	54	10	39	24	117	143
XXIV Norrbotten's »	6	94	32	11	2	1	30	140
	1016	429	467	317	178	180	3840	1571
Thereof in the towns {	72	13	108	34	14	10	741	179
	7%	3%	23.1%	10.7%	7.9%	5.6%	19.3%	11.4%

<sup>1</sup> One more case was notified, but this patient fell ill in the county of Örebro.



limited space, and during a period of 14 days. During the month following no more cases appeared to have occurred in this part but towards the end of summer a focus of about 50 cases made its appearance in this and neighbouring parishes.

In the beginning of April the first cases of an epidemic that registered about 40 cases occurred near the Norwegian boundary (Hotagen) in the county of Jämtland (XXII). Simultaneously there appeared in another mountain district of the county of Västernorrland, and far from the first named place, 5—6 cases within a short space of time, all of them in different families in 2 neighbouring villages (XXI).

Towards the end of April and in the beginning of *May* an epidemic had also broken out in Stockholm.

The foci that later on developed in some of the above mentioned counties and in the county of Stockholm (I) during the latter part of the year were amongst the largest observed during the epidemic of 1911.

In *June* a distinct epidemic appeared in the South of Sweden, in the county of Älfsborg (XIV), this being also located to a part, where subsequently one of the largest epidemical centres of that year occurred. In the same month the first epidemic accumulation of cases of poliomyelitis occurred in that county of the south part of Sweden (the county of Jönköping, V) which later developed into the most extensive of all the foci. In the month of June signs of an epidemic were also observed in the county of Kopparberg (XIX), while it was not until the month of *July* that the disease may be said to have assumed an epidemic character in the 2 counties situated northwest of Stockholm (Uppsala (II) and Västmanland (XVIII)).

In *August* cases of poliomyelitis began to be more numerous in the counties of Södermanland (III), Östergötland (IV) and Västerbotten (XXIII). Also in the two most southern counties (X—XI) the cases were by this time (July—August) becoming more numerous. Last of all the epidemic reached the counties of Kalmar (VII) and

Kronoberg (VI). It was not until *September* that the disease here acquired an epidemical character. During this month none of the 24 counties of Sweden were free from acute cases.

From the above it will be seen that whereas in the Northern, Central and Southern Sweden large parts of the interior of the country as well as the counties along the East coast were visited, the majority of the counties along the Southern and Western coast have been comparatively spared by the epidemic of that year.

The curve formed by the cases registered every month during the epidemic of 1911 scarcely displays anything remarkable. It is the ordinary picture of the course of an epidemic of infantile paralysis with its typical, rapid and powerful rise during the summer months. The maximum was reached in September, while in 1905 the summit was already reached in August. During the month of September 1911 more cases were recorded than during the entire year of 1905.

In the same way as the first large epidemic (1905), comprising the whole country, did not die away with the entry of the cold season, we see the epidemic of 1911 extend on to 1912. During the first months of this latter year the curve remains at a comparatively high level. But while in 1906 the maximum was reached in January, we find during the month of July 1912 an alarming rise (416 cases registered), by far exceeding the highest point of the curve of 1906 which was reached in January. The curve reaches during July 1912 even higher than it has ever done before in our country at this time of the year.

In some limited districts the infantile paralysis did not appear in epidemics until the approach of winter. This in especially the case in Gothenburg, as will be seen

Table II.

Number of cases of Infantile Paralysis observed  
in Sweden during 1911.

	Jan.	Febr.	March.	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Date of onset not known	Total number of cases 1911
Stockholm's town	1	5	1	3	19	23	11	24	57	32	17	11	—	204
I Stockholm's county	—	5	—	—	2	7	1	25	54	42	34	5	—	175
II Upsala                »	—	—	—	—	—	—	13	7	15	31	—	1	—	67
III Södermanland's »	—	1	—	3	—	3	—	8	23	32	8	10	—	88
IV Östergötland's »	—	—	—	2	2	2	—	31	36	47	45	13	—	178
V Jönköping's        »	—	1	—	—	—	4	49	414	313	142	101	41	—	1065
VI Kronoberg's       »	—	2	1	2	—	1	—	5	21	31	20	5	—	88
VII Kalmar            »	—	—	2	2	—	—	—	2	38	67	61	41	6	219
VIII Gottland's       »	—	—	—	—	—	—	—	4	8	—	—	2	—	14
IX Blekinge           »	—	—	—	—	—	—	—	—	4	4	2	1	—	11
X Kristianstad's     »	—	—	—	—	2	—	—	4	9	19	5	4	—	44
XI Malmöhus          »	—	—	—	—	—	—	—	—	—	—	—	—	—	—
a) Malmö town	—	—	—	—	—	—	—	—	2	1	—	—	—	3
b) the rest of the county	—	—	2	—	—	2	8	14	21	25	21	9	—	102
XII Halland's               »	—	—	—	—	—	—	2	1	19	1	3	1	—	27
XIII Göteborg's & Bohus »	—	—	—	—	—	—	—	—	—	—	—	—	—	—
a) Göteborg's town	—	—	—	—	—	—	—	1	1	3	11	14	—	30
b) the rest of the county	—	—	—	—	—	—	—	—	2	9	8	5	—	24
XIV Älfsborg's county	—	2	—	—	2	17	34	106	103	32	31	14	—	341
XV Skaraborg's        »	—	—	1	—	—	—	2	6	35	36	26	8	—	114
XVI Värmland's       »	—	—	—	2	2	2	4	3	9	1	2	2	—	27
XVII Örebro            »	—	—	—	—	—	1	2	2	5	5	5	11	—	31
XVIII Västmanland's »	—	—	1	—	5	—	15	57	55	35	25	6	—	199
XIX Kopparberg's     »	—	—	—	—	1	8	1	35	51	14	13	7	—	130
XX Gäfleborg's        »	—	1	3	4	1	1	4	10	28	34	6	3	3	98
XXI Västernorrland's »	—	—	—	2	13	8	28	98	90	53	7	1	—	300
XXII Jämtland's        »	—	—	—	3	35	3	5	16	33	16	3	—	—	114
XXIII Västerbotten's »	1	—	—	—	4	—	—	17	29	34	24	8	—	117
XXIV Norrbotten's    »	—	—	1	1	—	1	—	3	6	1	5	12	—	30
Total	2	17	12	24	88	83	179	893	1067	747	483	235	9	3840

from Table III. Not until October and November did an epidemic flare up in this town reaching its maximum in December and January. The epidemic

Table III.

	Jan.	Febr.	March	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
Stockholm 1911 . . . .	1	5	1	3	19	23	11	24	57	32	17	11
» 1912 . . . .	6	—	—	2	3	2	3					
Göteborg 1911 . . . .	—	—	—	—	—	—	—	1	1	3	11	14
» 1912 . . . .	15	6	8	8	13	7	20					

in Gothenburg shows, besides, a very protracted and variable course. After a temporary decline in early summer 1912, a new rise took place towards the later part of the summer. Also in another respect the Gothenburg epidemic differed from the common type. When an epidemic had broken out within a limited area we observe, as a rule, a gradual or often rapid ascent followed by a continual and rather sharp decline of the curve leading to a comparatively rapid extinction of the epidemic. Also in Stockholm the curve shows a similar irregular course. Here two maxima are observed, one during the spring and the other in late summer. With regard to the country, a similar curve characterises the above mentioned epidemic in Färila and neighbouring districts.

#### The roots of the epidemic.

Of great interest, naturally, is the question of the root and origin of the epidemic. Did it flow from one common spring or had it its source in several fountain springs? This is the question which first forces itself upon us and which deserves closer attention.



As will appear from Table II, solitary cases of poliomyelitis have occurred during the first months of the year 1911 in most of the counties of Sweden. They are, however, less numerous than has generally at this time of the year been recorded in this country during the majority of the 6 years that have passed since the appearance of the first large epidemic (1905). With regard to the number of cases during 1910 it falls to a value which, practically speaking, is identical with the minimum of the curve of infantile paralysis reckoned from and including 1905.<sup>1</sup> In many of the counties which were severely visited during 1911 the number of cases of poliomyelitis observed during 1910 fell below the number observed the same year in some of the counties that were least affected during the epidemic of 1911. Thus only one case was notified during 1910 from each of the counties of Älfsborg and Kalmar, which were so badly ravaged during 1911, while the counties of Värmland and Gothenburg, which during the epidemic of 1911 were only very slightly affected were represented in 1910 by resp. 10 and 4 cases (Table I).

The appearance of the cases of infantile paralysis, during 1910 and the first months of 1911 give no definite explanation with regard to the situation of the nearest

<sup>1</sup> It may be remarked that the figures to which reference is made here and in the following are to be regarded as only approximative. As no compulsory notification of the cases has existed after the big epidemic of 1905, it is not excluded that some cases may have occurred during these years which have not been reported. Considering, however, the very lively interest which has always manifested itself in our country with regard to all questions bearing upon infantile paralysis ever since the first large epidemic, it is very probable that the official figures here stated in the main reflect the real conditions. Nothing seems to prevent their being used even though with some slight degree of reservation as the basis for a study of the prevalence of infantile paralysis in our country during the past years.

source of infection. Nothing seems to point to the supposition that, as the nearest cause of this great epidemical outbreak, we should at all have to reckon with a *common* source of infection, as regards time located to the period nearest preceding the epidemic of 1911.

Nor can it be said that a closer analysis of the first touches of the approaching epidemic are adapted to give rise to a supposition that it originated in some common source of infection located to some certain district of the country. On the contrary it renders such a supposition rather improbable.

The four previously mentioned places, where an epidemic amassment of cases of infantile paralysis occurred early in the spring, are situated at about 20 to 30 (Swedish) miles distance from one another, and the three northern ones are not situated near any high roads. The two situated farthest north are mountain villages lying far away from any more closely inhabited place, and besides, during this part of the year the communication with the outer world is, owing to the physical conditions prevailing, still more reduced than later on, when the snow and ice have melted, being in fact minimal.

Stockholm can, no doubt, with more aptness be considered a plausible source of infection, as the communications of this city with other parts of the country are livelier than those of any other place. As far as the 3 above mentioned places in the North of Sweden are concerned, the groups of cases appeared somewhat *earlier* than the outbreak of the epidemic in Stockholm.

Still the assumption is plausible that the groups of cases which appeared later in the spring and during summer were, in many cases, secondary to already

existing foci. That such has been the case can in fact with certainty be proved in a number of cases. But it is to a certain degree surprising that in the three counties nearest Stockholm and the county of Stockholm no epidemic occurrence of infantile paralysis can be traced until the epidemic had been raging in Stockholm for several months. With regard to the county of Upsala (II) the epidemic had already raged in Stockholm for two months before the first case of the epidemic was observed within this county, this case being at the same time the first observed here during that year.

It will be evident from what has been said, that the first four epidemical accumulations of infantile paralysis during 1911 cannot very well be regarded as having originated from some common source of infection located to any special district. It has under no circumstances been possible to establish an origin of this kind.

If we recollect that during each of the years 1906—1911, a rather large number of sporadic cases or small groups of cases and small epidemics have occurred, and further that they have occurred scattered and in far distant places all over the country, it is hardly possible to arrive at any other conclusion than that the infective agent has not only survived from year to year within our country but also that it must have acquired a wide-spread distribution. Much more plausible than the idea of a common source of infection to the great epidemic of last year seems, under such circumstances, the assumption that the epidemic originated in several widely separated districts. From reasons which we have not yet been able to discern, but probably to be found in the biological characters of the virus of poliomyelitis, the infective agent existing in

different parts of the country is likely to have increased in virulence, a number of foci arising in loco, and from these latter the infection has been conveyed further.

The more sporadic cases or epidemics which have occurred in this country since 1905, are probably to be considered as remnants and offshoots of the great epidemic of that year.

If the above reasoning be correct — and at more than a presumption in one or another direction regarding the origin of the epidemic we cannot arrive — the second large epidemic of infantile paralysis in our country should consequently be considered to rest on a basis the roots of which had an intimate connection with the large epidemic of 1905. Most probably the large epidemics also stand in the same genetic relation to each other as do the individual cases in the smaller foci. But just as here the genetic relation cannot always be fully demonstrated, in the same way are the connecting links of the great epidemics hidden from us. It is only now and then that in the sporadic cases we discern the separate link in the chain of the transplantation of the virus, which, all too frequently hidden, we are compelled to assume as constantly taking place.

#### **The relation between the towns and the country.**

It has been pointed out as a characteristic of infantile paralysis that the disease preferably attacks places lying far away from the larger centres, visiting villages and farms situated in out-of-the-way places, at the same time appearing to evade the cities and more densely populated places. Numerous examples of this have been observed during earlier epidemics, in our country as well as elsewhere. Repea-



ted experiences in this direction have been made also during the last epidemic. But the exceptions to this rule are obviously so numerous that they necessitate a closer investigation regarding the relation of this epidemic to the towns and the country.

In 1905, as distinctly pointed out by Wickman, no epidemic outbreak of infantile paralysis occurred in any single town of the whole country. Only scattered cases were observed. The greatest number of cases registered in any town during 1905 was in Stockholm, but there the cases amounted in that year to only 10. *Quite different is the case during the epidemic of 1911.* Particularly noteworthy is the fact that rather considerable epidemics have occurred in the two largest cities of Sweden, Stockholm and Gothenburg. Thus the disease acquired in Stockholm an epidemic character, comprising about 200 cases. In Gothenburg, where the epidemic did not make its appearance until towards the end of 1911 more than 100 cases have occurred up to Aug. 1912 (see Table III).

Also in other towns the cases accumulated until they gave rise to by no means inconsiderable epidemics. Thus in Huskvarna, Eksjö, Jönköping and Västerås 94, 68, 55 and 44 cases resp. were recorded last year.

Wickman estimates the total number of cases observed in the towns during 1905 at 72, which hardly amounts to 7 % of the whole number of cases observed that year. In 1911, on the other hand, 741 cases were observed in the towns of Sweden. This number represents 19.3 % of all known cases of that year. If market-towns and municipalities, which in their administrative organisation are more like towns than rural parishes, are included, the number of cases observed

within the towns and similar administrative units rises to about 900. This makes no less than about 25 % or, in other words, about one-fourth of all the cases recorded during that year. But as the population of the towns and corresponding places constitutes, in round figures, one-fourth of the population of the whole country, it will at once be evident that if the cases that occurred in the towns and town-like places are compared with the number of people living in them, and the cases observed in the rural districts to the country-population, the epidemic of infantile paralysis during 1911 *has not* — as in 1905 — preferably ravaged the population living in the country. *It will be found that last year the population of the towns and similar places was attacked to about the same extent as was the folk living in the country.* It is, however, of great importance that the significance of these facts be rightly valued. If the different places which were visited by the epidemic of 1911 are compared with each other, we find that it is amongst the country parishes that the greatest percentage of sickness is to be found. With regard to the others it looks generally as if a greater proportion of the population living in the small and middle-sized towns than in the large towns has been attacked. In order to confirm these statements reference may be made to the annexed tables. Table IV contains details in this regard from the majority of the towns in which poliomyelitis may be said to have acquired an epidemic character during 1911. In Table V some of the most ravaged country parishes are recorded for comparison.

From the tables it may be gathered, inter alia, that in those towns — Eksjö and Huskvarna — in which the disease ravaged most severely it has,

Table IV.

T o w n s .	Population.	Number of cases of Infantile Paralysis <sup>1</sup> .	Percentage attacked.
Stockholm . . . . .	346,599	210	0,06
Göteborg . . . . .	170,606	107 <sup>2</sup>	0,06
Norrköping . . . . .	46,629	15	0,03
Jönköping . . . . .	27,226	60	0,2
Upsala . . . . .	26,586	14	0,05
Westerås . . . . .	19,803	44	0,22
Sundsvall . . . . .	16,894	22	0,13
Kalmar . . . . .	15,722	18	0,1
Visby . . . . .	10,022	13	0,13
Huskvarna . . . . .	6,237	97	1,4
Eksjö . . . . .	5,332	68	1,28
Tidaholm . . . . .	4,608	19	0,4
Ulricehamn . . . . .	2,324	17	0,73

nevertheless, attacked a smaller percentage of the population than it has done in some country parishes belonging to the same focal area or to foci in other counties.

A closer investigation thus shows that the remarkable difference between the epidemics of 1905 and 1911, with regard to the relative devastation among the inhabitants of the towns and the country, in reality only constitutes a displacement of the proportions, not an inversion or a levelling of the same. In 1911 as well as in 1905 the disease, as a rule, has shown an inclination to attack a greater number of people living in the country than of those living in

<sup>1</sup> Here are included also those cases that have occurred during that part of 1912 during which the epidemic has still continued in respective towns.

<sup>2</sup> Number of cases including July 1912. The epidemic continues in Gothenburg.

Table V.

Parishes.	Population.	Number of cases of Infantile Paralysis.	Percentage attacked.
<i>Jönköping's county:</i>			
Bellö . . . . .	446	10	2,2
Nåshult . . . . .	630	13	2
Medelby . . . . .	674	22	3,3
Beckseda . . . . .	898	26	3
Svarttorp . . . . .	910	18	2
Kråkshult . . . . .	963	20	2
Nye . . . . .	975	21	2,1
Barkeryd . . . . .	1,257	33	2,6
Eksjö country parish . . . . .	1,298	26	2
Hult . . . . .	1,314	33	2,5
Björkö . . . . .	1,316	24	2
Höreda . . . . .	1,560	68	4,3
<i>Östergötland's county:</i>			
Grebo . . . . .	1,142	25	2,2
<i>Älfsborg's county:</i>			
Borgstena . . . . .	705	14	2
Örsås . . . . .	1,053	18	1,7
<i>Västernorrland's county:</i>			
Attmar . . . . .	3,122	51	1,6

towns and similar places, but the difference in this respect between them has been considerably less in 1911 than in 1905.

The reason of this varying behaviour on the part of the two large epidemics comprising the whole country of Sweden can scarcely be fully ascertained. It might be presumed to depend upon a different degree of virulence in the infective agent, that this possessed a higher degree of virulence during the last big epidemic than during the former. But it may be remarked that during the period 1906—1910, during



which our country was spared larger epidemics, and virus consequently could not be considered possessing in general any very high degree of virulence, the relation between city and country has been somewhat varying during different years as will be seen from Table I. Even if the percentage of cases occurring in the towns during this period, as a rule remained at a low figure, often lower than in 1905, we still find that in 1907 not less than 23 % of all cases notified that year occurred in the towns. This figure thus exceeds by a slight percentage the one found to pertain in regard to the real towns during the epidemic of 1911. The said year (1907) the largest number of cases occurred in the two southernmost counties, i. e. no less than 163 out of the 467 cases recorded from the whole country. Of the 90 cases observed in the county of Malmöhus, no less than 45 belonged to the towns, making in all 50%. They were divided amongst 5 of the 8 towns of the county.

### Topography.

Wickman and others after him observed a certain regularity with regard to the mutual distribution of the separate cases in an epidemic. Marked out on the map, they are easily collected in larger and smaller foci between which only a few scattered cases occur. But even these latter are, as a rule, found in the vicinity of the larger foci. This characteristic picture holds good also in the case of the epidemic of 1911. Also with regard to the nearer details and the relation between the different cases the present epidemic shows full analogy to what is already known. A more de-

tailed description of these conditions may therefore be omitted here.

One of the foci of 1911 (see map 3) offers, however, in many respects much of interest and may on that account be worth a more detailed description. On account of its large size it is apt to draw attention, extending as it does over large areas of the counties of Jönköping (V) and Kalmar (VII) and covering with its outposts towards the northeast and southwest a stretch of land nearly 16 (Swedish) miles in length. When the solitary cases are mapped out an obvious concentration and evenness with regard to their distribution within the central area in the county of Jönköping is disclosed. The peripheral zone, on the other hand, which extends over great parts of the county of Kalmar and smaller parts of the counties of Östergötland (IV) and Kronoberg (VI), dissolves into groups of more independent or irregular strokes or areas and solitary cases. This single large focus comprises about 1300 cases, and thus alone includes more cases than the whole of the country-epidemic of 1905.

The principal interest connected with this focus from an epidemiological point of view lies in its manner of growth. The first origin of this large epidemic centre is to be sought for in the town of Eksjö, a military station situated by the railway. Already in the middle of June a case occurred here in the family of a craftsman employed by the Railway Company. A direct or indirect connection with any source of infection could not be discovered. Within the whole county of Jönköping only one single case had occurred up to that date, viz. in the town of Jönköping in February. The first case in Eksjö was soon followed by two more in the same family. Before the end of the month of

June a fourth case had occurred in a family which had been in contact with the first family. After that new cases appeared continually during July and August, whereas by the end of September the epidemic in this town may be said to have become extinguished.

Already in the month of July cases occurred in different parishes belonging to the medical district of Eksjö. Also in the district of Hvetlanda, situated south of the former, a number of cases were observed at this time. During August the epidemic flared up in full force within these two medical districts. Altogether 300 cases were recorded during this month. By this time the epidemic had already spread westwards from Eksjö to the neighbouring medical districts of Nässjö and Jönköping, and towards the end of the month some cases appeared also in Vrigstad district in the south-west direction. During September the epidemic spread further still, now appearing — the cases being, however, less numerous —, northwards in Tranås, and in the district of Boxholm and Kisa of the county of Östergötland. Eastwards it reached Wimmerby and Mållilla district in the county of Kalmar and southwards Högsby district. During the last days of September Grönskåra district was reached; the districts of Åsheda and Växiö, both situated in the county of Kronoberg being also attacked during September. In October the epidemic crept still further eastwards, reaching the medical districts of Mörtfors and Stranda on the Baltic coast. And finally in November and December, during which time a good many cases occurred, the boundary extended somewhat farther west, north and east.

More clearly than words a look at the annexed map 3 will give an idea of the main features of the manner of growth of this epidemic. On the map the

most peripheral cases which have occurred up to and including resp. June 30, July 23, Aug. 22, September 30, October 31, November 30 and December 13 are marked out. All cases belonging to the different series are connected with a line thus representing the utmost boundary of the spread of the epidemic at the periods of time indicated. Of the c:a 1300 cases that occurred the dates of onset of the disease is unknown in about 10. Of the remainder there is only one which, in regard to time, falls outside the area to which it ought to belong, according to the limits marked out on the map. This case occurred within Vrigstad district during June, and not until two months later did new cases appear there. It is indicated on the map by a cross.

The investigation of this focus shows, consequently, that the epidemic, seen on a large scale, like an overflowing river, month by month spreads over neighbouring, previously unattacked areas, gradually placing new zones like concentric rings around the older areas. When the epidemic has reached the extension marked out for the month of September it is already extinguished in the centre (town of Eksjö).<sup>1</sup> But like a ring-worm patch it continues incessantly, and more especially towards the East, its peripheral advance until it ceased towards the end of the year, partly owing to the fact, that it had now reached the sea coast.

With the knowledge we now possess as to the existence of the virus in the mouth and pharynx of patients, as well as of healthy individuals in the surroundings of those attacked, there seems to be no more acceptable explanation for this manner of growth than that all around the periphery of an epidemic, owing to the

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<sup>1</sup> After the month of September only 2 cases (in November) were observed in this town during 1911.



contact between the inhabitants of neighbouring places, the infection is slowly but surely carried from one individual to another to more peripheral parts.

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As was mentioned above, it is obvious that the great epidemic which began in 1911 is not yet over. The disease continues its ravages in our country this year also, thereby constantly involving new territories while the districts visited last year have hitherto been almost entirely spared. Such a continuation or fresh flaring-up of an epidemic during the subsequent year, as well as the fact that the cases then generally are located to other parts than those visited the previous year, has been observed also by other investigators. ZAPPERT<sup>1</sup> observed the same thing during the epidemic of 1908—1909 in Vienna and Austria. HARBITZ and SCHEEL<sup>2</sup> remark that during the epidemics in Norway, it has been the rule that a district which during a certain year had been visited by the disease was spared the next year. LOVETT and RICHARDSON<sup>3</sup> made similar observations while studying the outbreak of the epidemic in Massachusetts during 1907—1910. They also point out that the disease showed a tendency to flare up in greater country-epidemics every other year, »two-year periodicity», and an inclination to revisit every second year a place that

<sup>1</sup> ZAPPERT. Studien über die Heine-Medinsche Krankheit (Poliomyelitis acuta), Leipzig u. Wien, Fr. Deuticke 1911.

<sup>2</sup> HARBITZ und SCHEEL, Patologisch-anatomische Untersuchungen über akute Poliomyelitis und verwandte Krankheiten, Videnskabs-Selskabets Skrifter, Christiania 1907.

<sup>3</sup> LOVETT and RICHARDSON. Infantile paralysis with especial reference to its occurrence in Massachusetts 1907—1910. Monthly Bulletins of the Massachusetts State Board of Health for 1911.

has already been the seat of an epidemic, whereas in places less heavily afflicted, the disease seems to continue year by year with about the same number of cases.

Whereas the last mentioned investigators are inclined to explain the fact, that the epidemic does not visit the same district during two consecutive years as an expression of immunity attained by the inhabitants of the district visited, others again consider this explanation improbable.

»Man müsste«, ZAPPERT claims, »um dieselbe zu acceptieren, annehmen, dass in einer Bevölkerung von mehreren Tausend Menschen eine Erkrankungsziffer von etwa 50 bis 100 Fällen, wie wir sie vielleicht in Lilienfelder Bezirke im Jahre 1908 annehmen dürfen, genügt hätte, um auch ohne sichtliche Erkrankung eine durchgreifende Infizierung der Bevölkerung zu setzen«.

Of great interest, especially when we have to form a judgement on the question just mentioned, are the observations that result from a comparison between the localisation of the epidemical foci of 1905 and 1911.

As has been pointed out by WICKMAN with regard to the epidemic of 1905, four or five larger epidemical centres were observed during that year (see map 2), one in the county of Skaraborg (XV), one in the county of Kronoberg (VI), one or two in the county of Örebro (XVII) and in the boundary district between Södermanland (III) and Västmanland (XVIII), and finally one in the boundary-land between the county of Östergötland (IV) and Kalmar (VII).

A closer investigation of the epidemic of 1911 reveals, that *within none of the places which were the seats of the 5 principal centres of 1905 has the disease appeared epidemically during 1911.*

But it is still more remarkable *that in the neighbourhood of almost all of the former centres the scenes of the most intense devastations are to be found during 1911* (see map 2). For instance, not far south of the seat of the Skaraborgfocus of 1905 we find the most northern of the 3 or 4 almost continuous large foci in the eastern parts of the counties of Skaraborg (XV) and Älfsborg (XIV) in 1911.

In the county of Västmanland (XVIII) and in the county of Östergötland (IV) the foci of last year form, geographically seen, an almost direct continuation of the centres of 1905. In the province of Småland (V, VI and VII) the principal focus is situated between the places occupied by the Kronoberg- and Ätvidaberg-foci of 1905 and directly adjoining the former of these districts. Another of the large foci of last year, that in the county of Västernorrland (XXI) is chiefly situated directly south and west of a district, where rather many cases accumulated during 1905, although no distinct epidemic occurred then.

A comparison between the localization of the principal centres of the large epidemics of infantile paralysis thus displays, 1:0, *that in most places the new and old centres are immediately adjacent to each other*, and 2:0, *that, notwithstanding this, only a few scattered cases of infantile paralysis were observed during 1911 within the limits of the old centres, while, on the other hand, in 1905 only a few scattered cases occurred in those places which during 1911 became the seats of the large foci*.

Some figures will clearly illustrate these contrasts. The largest focus of the year 1911, here described in detail, comprised more than 1000 cases, as above stated. Within this extensive territory there occurred

in 1905 only about 50 cases, or, if the outpost to the county of Kronoberg be excluded, only about 20—25. The Kronoberg-focus — the largest during the epidemic of 1905 — situated in immediate proximity to the former, comprised about 250 cases. In 1911 there were scarcely more than about 10 cases observed within the same] area. The Skaraborg-focus of 1905 accounted for 120 cases, whereas during 1911 no more than 2 cases were observed within the same region. The foci in the counties of Skaraborg and Älfsborg in the year 1911, commencing just south of the 1905 Skaraborg-focus, comprised somewhat more than 300 cases, covering a territory in which only 14 cases were observed in 1905.

In view of these facts, which undoubtedly have a certain character of definite lawfulness, it occurs to one to ask whether or not this peculiar localisation of the foci of the epidemics of 1905 and 1911 is due to some close causal relationship.

On the one hand, the question arises whether the outbreak of some of the largest foci of 1911 in just those above mentioned places has not something to do with the fact that in 1905 epidemics visited more or less adjacent districts. That any more obvious connection can not be traced is evident from what has already been said with regard to the origin of the epidemic of 1911. But perhaps the possible existence of such a connection should not on this account be left out of mind.

On the other hand, one cannot but help looking for some definite, more common cause behind the fact, that in spite of the very close proximity to several of the largest foci of 1911, the epidemic of that year has not met with any greater dissemination



in the old centres (of 1905), once so fertile for an epidemic outbreak of the disease.

It may certainly seem less acceptable to many that we really should have to count with an immunisation of almost the entire population in a district where once a larger center has formed. As ZAPPERT remarks, it can hardly be possible that the immunisation of thousands of persons should take place with a figure of morbidity reaching only to some 50 or 100. Taking into consideration that 5 or 6 years have passed between the two large Swedish epidemics and that, besides, a new generation has been born and had time to arrive at that age, when it is most predisposed to become victim of the disease, the theory of a widespread, general immunity in the former epidemical centres as the result of the epidemic of 1905 may perhaps at first view seem still less plausible. Neither has one the right to assume a gradually continuing immunisation occurring chiefly or in great part during the years subsequent to 1905. Especially as those cases which, according to accessible reports, have occurred at the seat of the old foci during the interval between the two epidemics, are much too few in comparison with those of the first large epidemic, to justify such a conclusion.

The reports from Tingsås district in the county of Kronoberg (VI) will in this respect form an illustration. Owing to the unusually great interest with which the medical officer of health of this district, Dr. Brorström, has followed the whole question of infantile paralysis, it may be presumed that scarcely any case of this disease, that has occurred in his district ever since 1905, has escaped observation. From the annexed map 4, it appears that the number of cases registered

during this period has been rather small. During the great epidemic which commenced in 1905 about 190 cases were observed in Tingsås district, during the 4 years 1907—1910 only 43.<sup>1</sup>

As regards 1905 the figures are based upon records collected by WICKMAN, but in the case of the following years upon reports that Dr. BRORSTRÖM has kindly placed at my disposal. The striking difference between the year 1905 and the following years becomes still greater if the figures given by Dr. BRORSTRÖM are used also with regard to the former year. The principles according to which WICKMAN had planned his study of the epidemic of 1905 compelled him, even where for his own part he was fully convinced that they were true abortive types of infantile paralysis, to exclude some of the reported cases from his statistics.

On closer analysis, however, it is apparent that the view of the matter implying that a general immunity and non-susceptibility cannot exist in the former centres can hardly be correct. In order to make a correct estimation of this question several circumstances deserve to be taken into consideration.

With regard to infantile paralysis, the careful observations of WICKMAN had already made it probable that the contagion could be transmitted by individuals who were only slightly ill and showed no typical symptoms as well as by perfectly healthy persons. The correctness of this theory has been proved by the recent investigations of KLING, PETTERSSON and WERNSTEDT.<sup>2</sup> They have succeeded in demonstrating the existence of the virus in abortive cases and in healthy individuals living in the environment of typical cases of in-

<sup>1</sup> Owing to the fact that most of the cases that occurred during 1906 appeared in the first half of the year, it is evident that they belong to the epidemic of 1905, which in this district broke out in the latter part of the summer. I have therefore included the cases from 1906 in this figure.

<sup>2</sup> KLING, PETTERSSON and WERNSTEDT: Recherches sur le mode de propagation de la paralysie infantile épidémique (Maladie de Heine-Medin) Troisième Mémoire. Zeitschr. f. Immun. 1912.

fantile paralysis. Even if external circumstances limited these investigations to relatively small dimensions, yet the results obtained speak in favour of the view, that the dissemination of the virus amongst persons living in the surroundings of patients exhibiting typical symptoms, is very considerable. On account of the investigations made it may be reckoned that the number of abortive cases and virus carriers is often four or five times as great as the cases showing typical paralysees. Probably they are even more numerous than this.

The result of the above investigations make it probable that the susceptibility to an infection with the virus of poliomyelitis is rather small. Under such conditions we cannot but expect to find only a relatively *small* proportion of the population exhibiting clinical symptoms during an epidemical outbreak of the disease. With regard to infantile paralysis the same conditions evidently prevails as in the case of other infectious diseases *where only a slight degree of susceptibility is found to exist*, for instance, the epidemic cerebrospinal meningitis. In an epidemic outbreak also of this latter disease only a small proportion of the population is attacked, and bacteriological examinations have proved that also its virus is widely spread among the healthy individuals living in the surroundings of the patients.

The cause of this resistance to an infection with the virus of poliomyelitis is difficult to decide. KLING, PETTERSSON and WERNSTEDT have advanced the theory, that a great number of the people in certain places viz. greater towns have already earlier been subjected to an attack of this disease, the illness having only displayed the more general symptoms characteristic

of abortive cases. But the explanation can also be looked for in a congenital non-susceptibility or natural immunity. It is possible that both factors play a rôle.

Also another possibility must be taken into account which would be apt to protect non-immunized individuals within a district previously the seat of an epidemic. These individuals are, first of all, to be looked for among the children, and perhaps chiefly among the generation born since the preceding epidemic. The investigations of KLING, PETTERSSON and WERNSTEDT have pointed to the fact, that the contagion harboured by virus-carriers — whether convalescents after poliomyelitis or persons that have never fallen ill with the disease — probably possesses a lesser degree of virulence than the virus harboured by the real patients during the acute stage. Under such conditions it is probable that towards the end of an epidemic, and most likely for some time afterwards, the virus existing within a district once the seat of an epidemic would decrease in virulence.

From reasons readily understood, during fresh epidemics, it ought to be chiefly the grown up part of the population which imports the virus from infectious foci, not situated in its immediate proximity. Since it is, however, just this part of the population which has once witnessed an epidemic at home, it may be presumed that, on the whole, its various members will be less adapted as conveyors of a more virulent, and at the same time more infective virus. But under these circumstances the chance which the virus has of reaching, in a more virulent state, that more susceptible portion of the community which may perchance still be left or have grown up within an old epi-



demical centre, ought to be less than in those parts where the population has not yet been exposed to an epidemic of infantile paralysis.

It need not be specially pointed out, that the above reasoning in part rests on hypothetical grounds, but as it appears to be likely to facilitate the understanding of the disease, and at the same time seems rather probable, there may be sufficient excuse to bring it forward here. Under all circumstances it seems obvious that the small morbidity as compared to other epidemic diseases does not exclude the supposition of a general immunisation of that part of the population, that is susceptible to an infection, taking place within a focus of infantile paralysis.

On the other hand it is evident, that the above mentioned fact — which has also been observed by others — viz. that an epidemic of infantile paralysis has not appeared in a place ravaged during *the preceding* year, does not by itself justify the supposition that an immunisation of the population has taken place. Neither will this be proved by the fact that, when the disease flares up to a second country epidemic *after so long a lapse of time as between 1905 and 1911* it does not revisit the old foci. The cause of the different localisation might as well be due to circumstances of a more casual nature which are hidden from us. When, on the other hand, the circumstances are such as appear from *a comparison between the two large epidemics of 1905 and 1911*, the question has no doubt to be seen in another light. Thus it is noteworthy, as has already been pointed out, *that although in immediate proximity to almost all the old epidemic foci (of 1905) some district has been the seat of an epidemic during 1911 still no fresh outbreak has been observed to*

occur during the latter year (1911) in any of the foci of 1905. Still more important is the fact, revealed by a closer study, that some of the districts which were severely affected in 1905 were, during the epidemic of 1911, *almost entirely encircled by cases of infantile paralysis*. But notwithstanding this, they have themselves been left almost untouched by this later epidemic. For instance, the area occupied by the Kronoberg-focus of 1905, (see map 4), is bounded towards the north by the above mentioned outposts of the Eksjö-Hvetlanda epidemic and on the western border a marked epidemic-like accumulation of cases may similarly be found; also on the southern and western boundaries the solitary cases are lying more close to each other than those few that have occurred within the real limits of the old focus.

In view of such observations — and these are not the only that could be quoted — it seems that a more plausible explanation could hardly be suggested than that, *in spite of the interval of many years, and notwithstanding the fact that it was but a comparatively small proportion of the population that in 1905, within the foci then formed, showed clinical symptoms of the disease, in all probability there existed in 1911 none the less, in the part of the population, which then — 1905* — could be immunised, a general and wide-spread immunity against a renewed infection.

As regards the congenital immunity it may be conceived that the generation born during the interval between two successive epidemics this may be more general or more definite within districts once the seat of an epidemic outbreak than outside such districts.

The conclusions further indicate that those places which have once been severely affected by the disease

have all prospects of escaping a renewed severe outbreak of the epidemic, *even should this not occur until after the lapse of a series of years.*

The observations made in Sweden during 1905—1912 make this also presumable. At the same time there is no tendency to a biennial periodicity of the disease.

From the above it is evident that the observations made in Sweden during 1905—1911 regarding the relation of an outbreak of infantile paralysis to an area once severely devastated do not agree with the view obtained from a study of the outbreak of this disease in Massachusetts in 1907—1910, apparently the only country from which reports comprising material for several consecutive years have been published. It seems a matter for discussion whether this divergence with regard to the results obtained is not perchance more apparent than real. This question, however, will not be touched upon further.

Still another observation deserves mentioning. There are certain districts within which a considerable number of cases occurred in 1905, but where the cases were not grouped so closely together as to justify the name of an epidemic accumulation or focus.

This, is the case with the south western part of Södermanland (III) and the northern part of the county of Gäfleborg (XX). In these regions the cases of infantile paralysis have accumulated in large numbers also during 1911 (see map 2), in some places even developing into more or less distinct epidemics. In this respect, however, it is remarkable — as shown on closer investigation — that as a rule, it is not those localities within such an area that have been previously affected, that are attacked at the renewed appearance

of the disease within the same area, but as a rule other localities situated between those previously affected. This may also be observed to occur in regions, where the foci of 1905 and 1911 are somewhat overlapping (see map 4).

In connection with the investigations on epidemic infantile paralysis reference has often, and rightly, been made to analogies with the epidemical cerebro-spinal meningitis.

Before finishing this short study I should like once more to cast a glance at this latter disease. The more closely the nature of the epidemic infantile paralysis is studied, the more numerous will the points of resemblance be found that exist between this disease and the cerebro-spinal meningitis. There is, as a matter of fact, nothing that facilitates an understanding of the obscure points with regard to the manner in which the former disease most probably spreads as much as a comparison with the latter disease. It will then also be found that the whole line of development, along which the study of the epidemic cerebro-spinal meningitis has passed before the doubts regarding its contagious nature were dispelled, is followed, stage by stage, by the development which the study of the epidemic of infantile paralysis has hitherto undergone.

Cerebro-spinal meningitis also, just as later on was the case with epidemic infantile paralysis, did not at first give the impression of being a contagious disease. It also appeared at first only with scattered cases. And gradually these accumulated into small epidemics, as was the case with infantile paralysis in the eighties. After these came the large epidemics, fully comparable with the recent epidemics of infantile paralysis. It is not without some interest to point



out that especially from our country observations have been published from which can be concluded that similar topographical relations observed to exist between the centres of the two large epidemics of infantile paralysis in Sweden have also characterised the outbreaks of cerebro-spinal meningitis in our country. But also in other respects the large epidemics of meningitis show points which correspond to those that are characteristic of the large epidemics of infantile paralysis. The epidemical cerebro-spinal meningitis attacked only a small fraction of the population, and the districts which had once been traversed by the epidemic remained afterwards free for years. Mingled with the typical cases abortive cases occurred just as in infantile paralysis. The discovery of the meningo-coccus and its presence in the pharyngeal and nasal cavities of the patients placed the infectious nature of the disease beyond all doubt. Finally the discovering of the widespread existence of the virus also in healthy individuals made clear the obscure point which most of all spoke against the contagiousness of the disease — the difficulty or impossibility of demonstrating an obvious connection between the solitary cases. To this last link in an analogous chain of evolution the study of infantile paralysis has now likewise reached. Nobody who closely studies the real points and takes due regard to the facts already existing, is likely to escape finding that the eager study of the epidemic infantile paralysis has step by step revealed new facts, all of which are characteristic of contagious diseases. He will further find that what has hitherto seemed obscure is only an expression of the laws followed by the same diseases.

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## DESCRIPTION OF THE FIGURES

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- c. c. = central canal.
- i. p. = perivascular cellular infiltration.
- i. l. = leucocyte-neuronophagia.
- v. = blood-vessel.
- c. n. = ganglion cell.
- c. n. h. = hypertrophic glia cell.
- cap. = capillary.
- l. = leucocyte.
- p. = polyblast.
- e. = epithelium.
- ex. = exudation.
- p. = proliferating centrum.
- i. ly. = lymphocytic infiltration.
- d. = efferent duct of salivary gland.

- Fig. 1. Section of the lumbar enlargement of the spinal cord showing part of the anterior fissure, central canal and one of the anterior horns. *Macacus cynomolgus* no. 72 (page 69). Hardening in formalin and staining with haematoxylin-eosin. General view.
- Fig. 2. Section of the lumbar enlargement showing one of the anterior horns. *Macacus cynomolgus* no. 27 (page 40). Hardening as before; staining with haematoxylin, v. Gieson. Zeiss, obj. apochrom. 4 m. m., oc. comp. no. 6.
- Fig. 3. Section of the cervical enlargement showing part of one of the anterior horns. *Macacus cynomolgus* no. 22 (page 21). Hardening as before, staining with Weigert's iron-haematoxylin, v. Gieson. Magnification as before.
- Fig. 4. Section through the lumbar enlargement showing one of the anterior cornua. *Macacus cynomolgus* no. 55 (page 22). Hardening, staining and magnification as before.
- Fig. 5. Section of the spinal cord showing part of the grey matter. *Macacus cynomolgus* no. 129 (page 116). Hardening, staining and magnification as before.



- Fig. 6. Section of the cervical enlargement showing part of one of the anterior horns. *Macacus cynomolgus* no. 188 (page 128). Hardening, staining and magnification as before.
- Fig. 7. Freezing-section of the spinal cord of the same monkey. Glia-cell-neuronophagia in the anterior cornua. Treated according to Marchi, glycerine. Zeiss obj. 2 m. m.; immersion, oc. comp. no. 6.
- Fig. 8. Section through one of the tonsils of Johan Harald A—k (page 226). Hardening in formalin, staining with Weigert's iron-haematoxylin, v. Gieson. Zeiss obj. apochrom. 4 m. m., oc. comp. no. 6.
- Fig. 9. Section through the submaxillary salivary gland of Knut O—n (page 225). Hardening, staining and magnification as before.
- Fig. 10. Section through a large sized bronchus of Vera Elsa B—g (page 224). Hardening, staining and magnification as before.
-





*Fig. 1.*





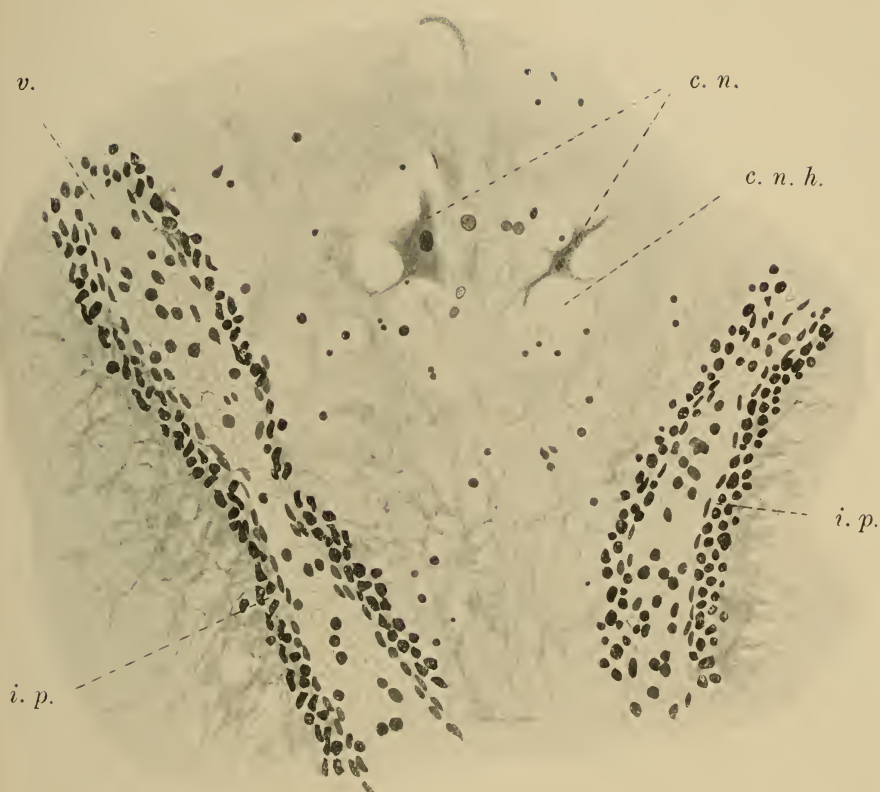


Fig. 2.





Fig. 3.

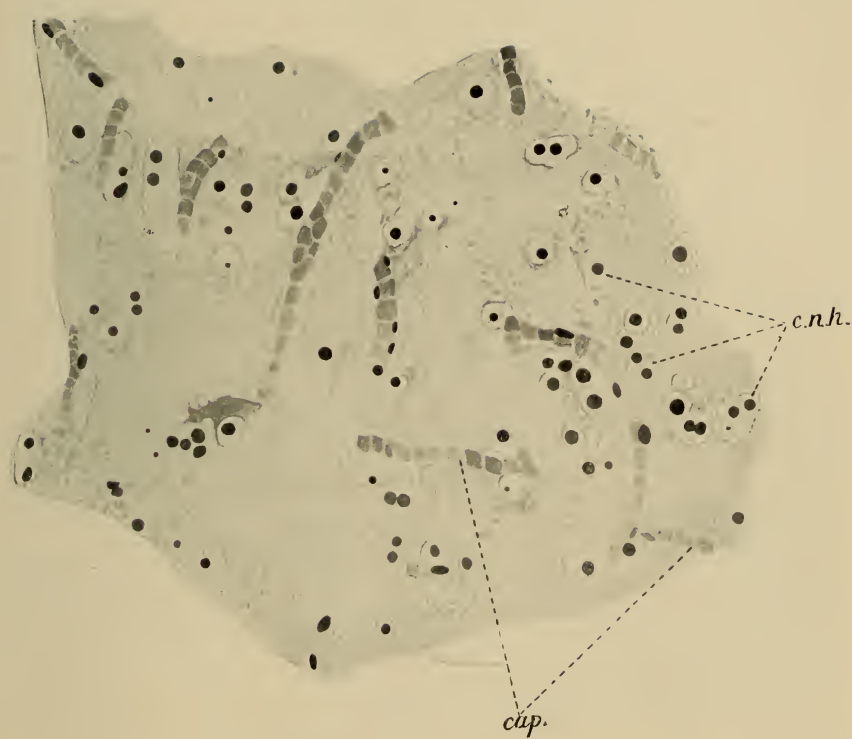






*Fig. 4.*





*Fig. 5.*

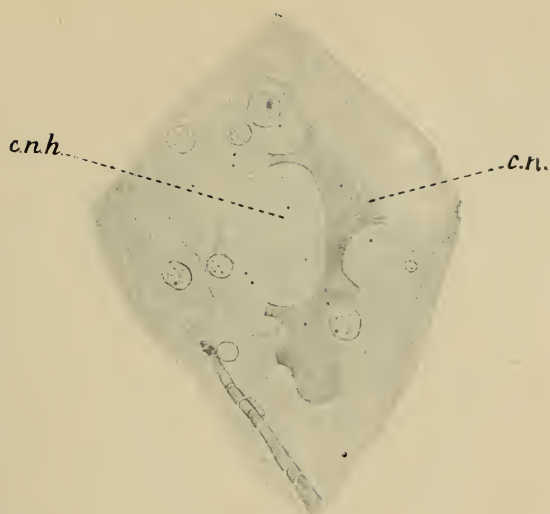






*Fig. 6.*





*Fig. 7.*



*Fig. 8.*



Fig. 9.

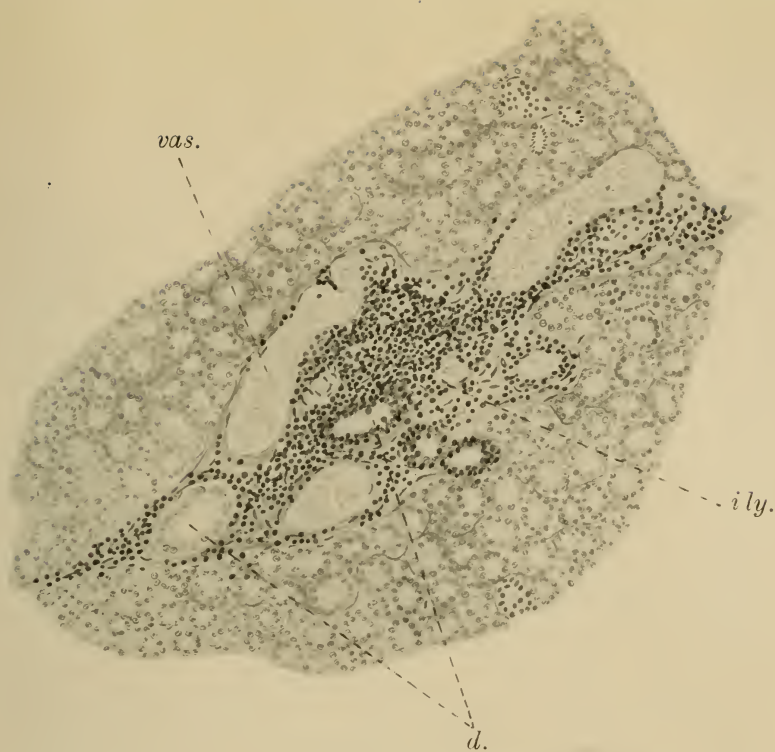
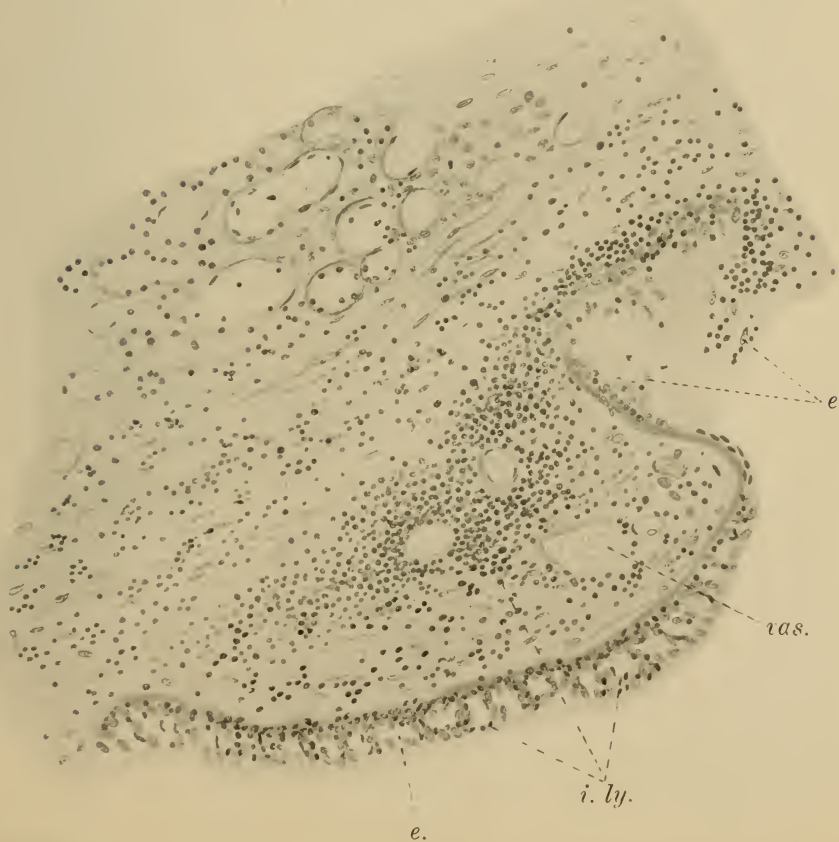


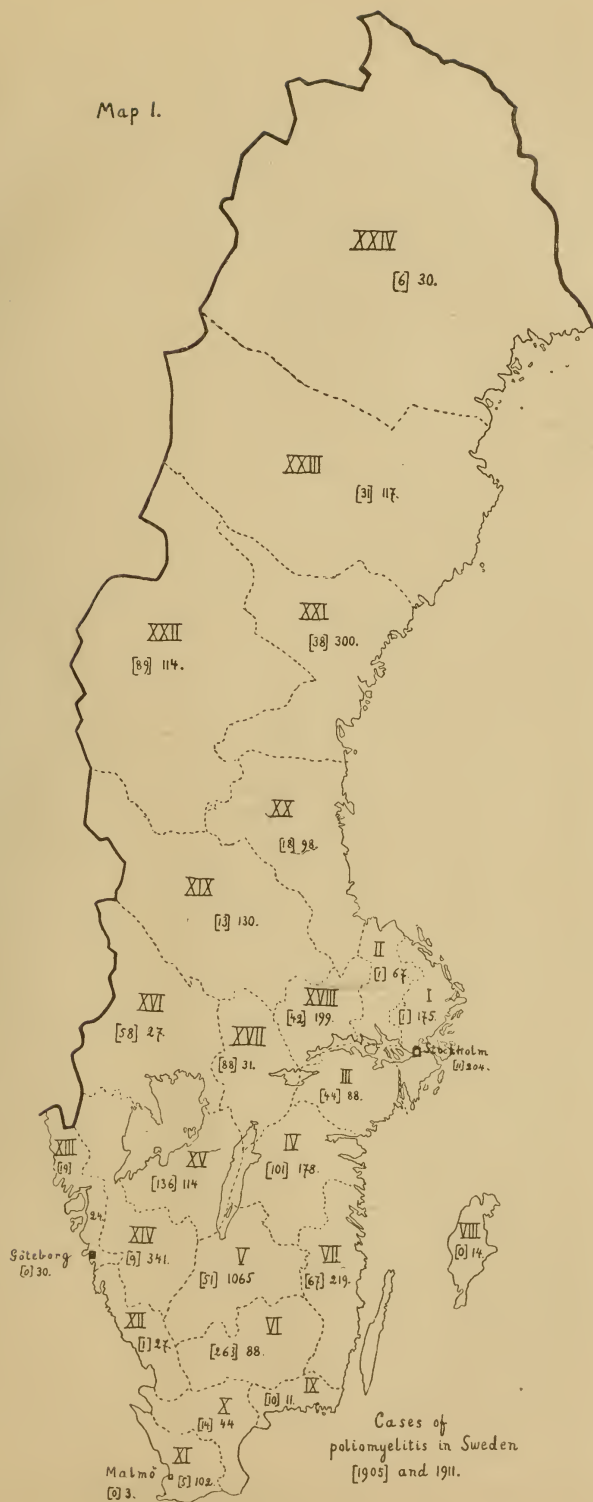
Fig. 10.







Map I.



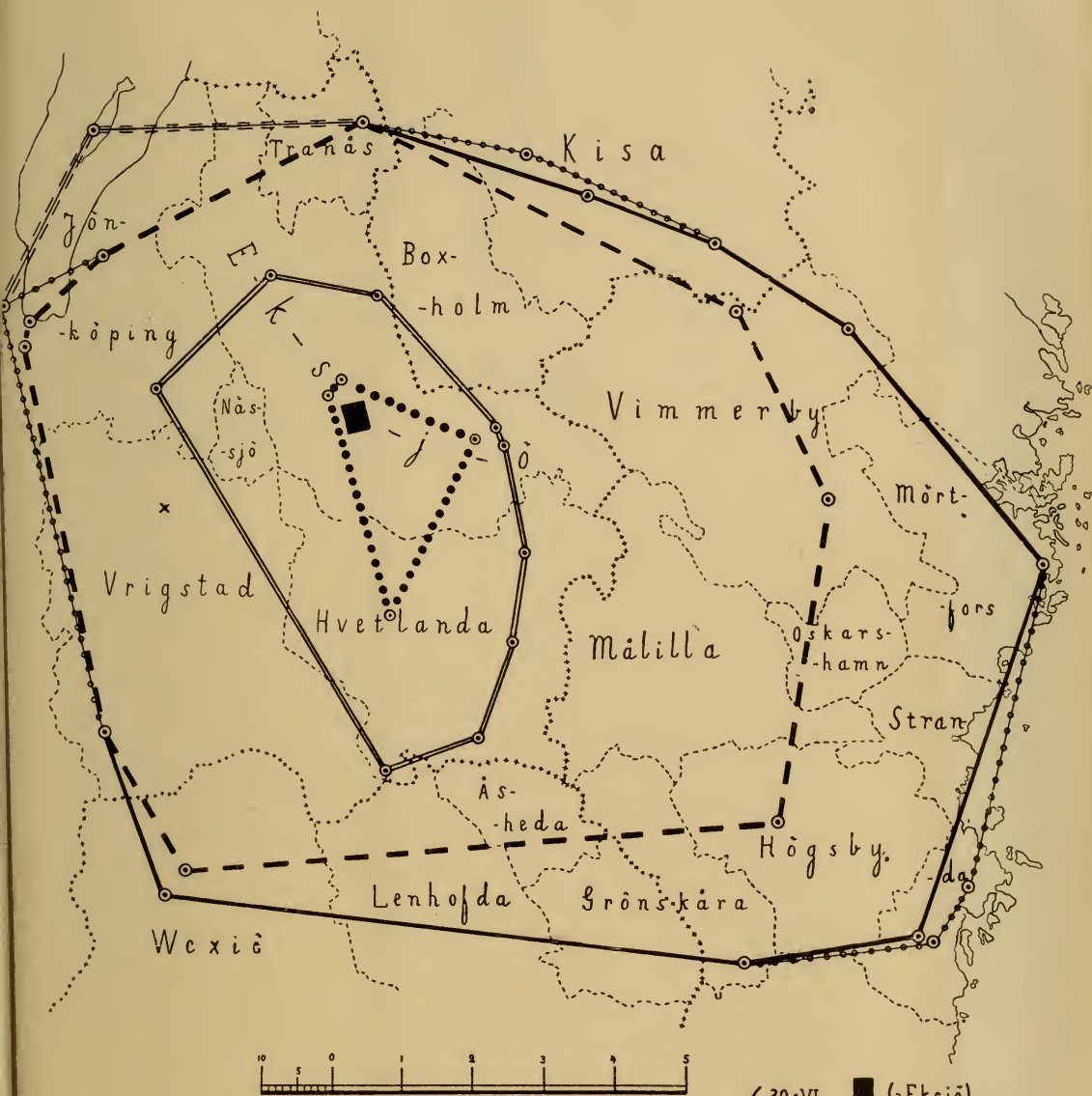
Cases of  
poliomyelitis in Sweden  
[1905] and 1911.









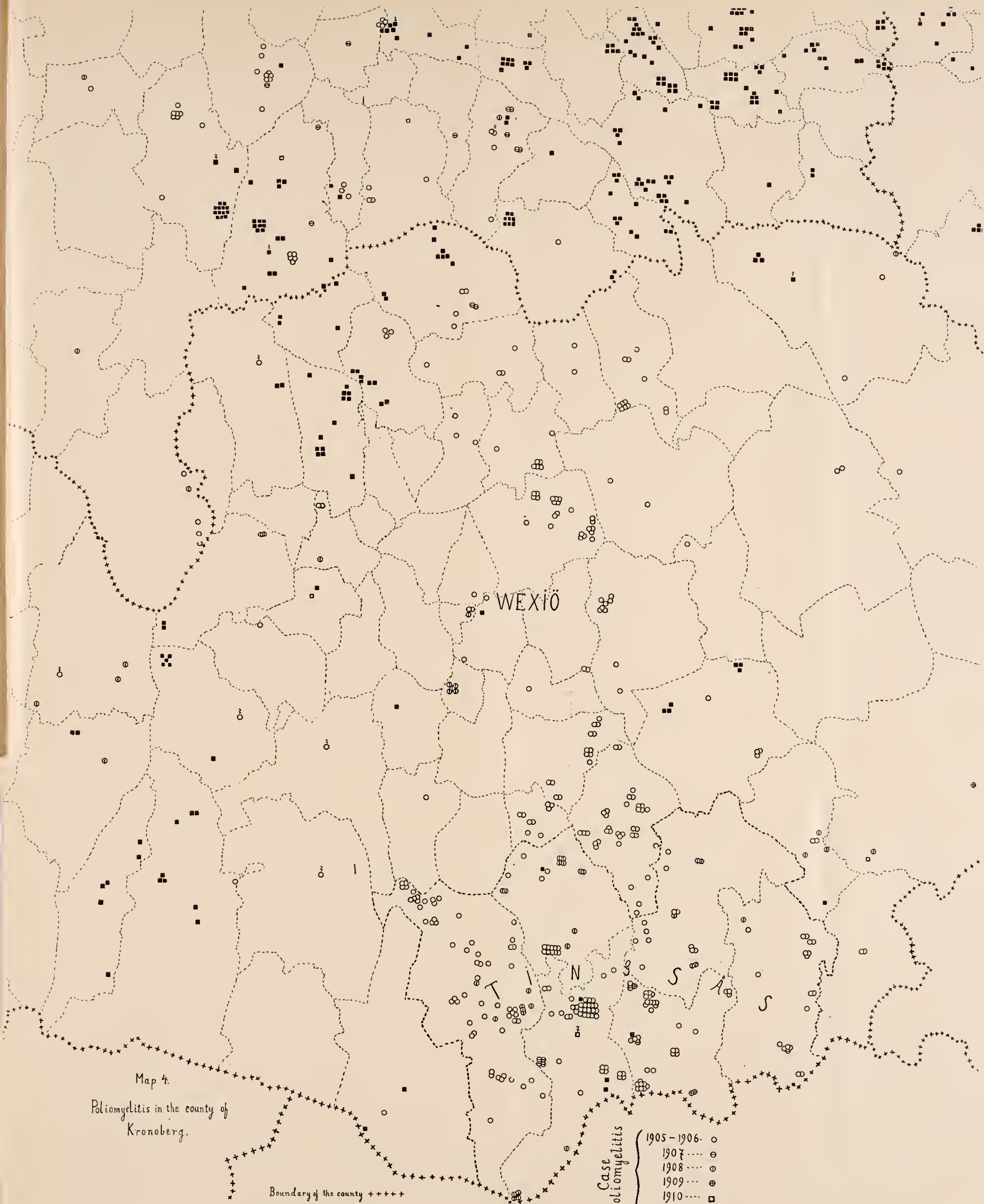


The extension of the epidemic of Eksjö-Hvetlanda on  
Case of poliomyelitis ○

Map 3.

30:VI	■ (Eksjö)
23:VII	●●●●●●●●
29:VIII	=====
30:IX	-----
31:X	=====
30:XI	○-○-○-○-○-○-○-○
13:XII	≡≡≡≡≡≡≡≡













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